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TABLE OF NORMAL VALUES

Albumin-globulin ratio.—1.5:1 to 3:1.
Amino acids.—5 to 8 mg. per 100 cc. of blood.
Base, total.—About 360 mg. per 100 cc. of serum.
Bilirubin, indirect.—Up to 1.5 mg. per 100 cc. of serum.
Bleeding time, capillary.—Three minutes or less.
Calcium.—8.5 to 11.5 mg. per 100 cc. of serum.
Carbon dioxide combining power of plasma.—Adults, 53 to 75 volu
children, 40 to 55 volumes per 100 cc.

...h rack from the water bath at
Record observed hemolysis and
...d Reporting."

	Serum Control	Reading
...sis	Complete lysis	NEG
	Complete lysis	DO

TABLE 3. URINARY FINDINGS IN CASES OF NEPHRITIS

Type of Nephritis	*Physical Findings*	*Chemical Findings*	*Microscopic F*
Acute nephritis	Quantity diminished, often very greatly. Color dark; may be red or smoky. Specific gravity, 1.020 to 1.030.	Urea and chlorides low. Much albumin: up to 1.5 per cent. Reaction acid.	Sediment abundant, red or brown, ular, blood and epithelial varieti cence. Erythrocytes abundant. cells. Few pus corpuscles.
Chronic glomerulonephritis	Quantity usually diminished. Color variable, often pale, and hazy. Specific gravity, 1.010 to 1.020.	Urea and chlorides variable. Largest amounts of albumin: up to 3 per cent. Reaction acid.	Sediment rather abundant. Many casts and casts of degenerated ep Blood present in traces: abundant Numerous renal epithelial cells s often free globules of fat and a few
Nephrosis	Quantity diminished. Color dark. Specific gravity, 1.020 to 1.040.	Urea and chlorides nearly normal, or high. Large quantity of albumin. Reaction acid.	Moderate number of casts, chiefly erythrocytes. Lipoid bodies usu
Nephrosclerosis	Quantity markedly increased, especially at night. Color	Urea and chlorides low in advanced cases. Albumin pres-	Sediment very slight. Few narro casts. No blood except in acute c

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COMPARATIVE EFFICACY OF AMEBACIDES AND ANTIBIOTICS IN ACUTE AMEBIC DYSENTERY

USED ALONE AND IN COMBINATION IN FIVE HUNDRED THIRTY-EIGHT CASES

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and
William W. Frye, Ph.D., M.D., New Orleans

The therapy of amebiasis is still a controversial issue and various amebacides have their individual proponents. Recently antibiotics have been added to the list of drugs demanding consideration. An unusual opportunity to observe the response of acute amebic dysentery to therapy occurred in the United Nations prisoner of war camp in Korea in 1951 when 644 patients with this disease were admitted to the hospital organized for the care of prisoners. Of these, 538 had uncomplicated acute infections and could be followed for a minimum period of six weeks.

The first report of the use of antibiotics in amebic dysentery was by Hargreaves,[1] who treated 57 patients with penicillin and noted some symptomatic improvement. Endamoeba histolytica trophozoites continued to be found in the stools, however. Improvement was interpreted as an effect on the secondary bacterial infection.

McVay, Laird, and Sprunt [2] reported the use of aureomycin in amebiasis. They treated 37 patients; 36 improved but in 4 E. histolytica reappeared in the stool. Armstrong, Wilmot, and Elsdon-Dew [3] treated acute amebic dysentery in 52 cases with aureomycin. The initial response in all patients was satisfactory, and ulcers healed rapidly. One month after therapy 27 were reexamined, and 7 had symptoms, rectal ulcers, and E. histolytica in the stools.

Most and Van Assendelft [4] used oxytetracycline ("terramycin") for 54 patients with amebiasis, most of whom were asymptomatic or only slightly ill. The stools of all became negative, but in one E. histolytica reappeared three months later. Five patients with severe disease responded "as well as with emetine." Following this, Tobie, Most, Reardon, and Bozicevich [5] treated all occupants in separate buildings of a mental institution, using bacitracin, aureomycin, or oxytetracycline; a single drug was used in each building. Though all patients were asymptomatic prior to therapy, 49% harbored E. histolytica. Oxytetracycline was found to be 100% effective in eliminating the organism on the basis of a six month follow-up, aureomycin was 60% effective, and bacitracin only 28% effective after 2.5 months.

Killough and Magill [6] reported results of treatment in seven cases of acute amebic dysentery with oxytetracycline. All of the patients complained of generalized abdominal cramps and bloody diarrhea with mucus. Repeated stool examinations revealed numerous motile trophozoites of E. histolytica. Proctoscopic examinations

† Lieutenant Martin died Sept. 27, 1951.

Senior Scientists, United States Public Health Service (Drs. Brooke and Weinstein). Professor of Tropical Medicine and Dean, Louisiana State University School of Medicine (Dr. Frye).

Hospital Corpsman Third Class Michael J. Sitiko, Fleet Epidemic Disease Control Unit No. 1, U. S. N., and Corp. Don Dimmock, 64th Field Hospital, U. S. Army, served as parasitological technicians in this study.

The following drugs were supplied by the makers for use in this study: aureomycin by Lederle Laboratories, Division of American Cyanamid Co., Pearl River, N. Y.; chloramphenicol by Parke Davis & Co., Detroit; oxytetracycline ("terramycin") by Charles Pfizer & Co., Brooklyn; and the combination of bismuth glycolylarsanilate and chloroquine diphosphate (milibis®-aralen®) by Winthrop-Stearns, Inc., New York.

The studies here reported were conducted by a "Joint Dysentery Unit" under the sponsorship of the Commission on Enteric Infections of the Armed Forces Epidemiological Board. The personnel participating in the study in Korea came from the Army Medical Service Graduate School, the Fleet Epidemic Disease Control Unit No. 1, the Microbiological Institute and the Communicable Disease Center of the United States Public Health Service, the 406th Medical General Laboratory, the 64th Field Hospital, the Bureau of Laboratories of the Florida State Board of Health, and the Louisiana State University School of Medicine.

1. Hargreaves, W. H.: Chronic Amœbic Dysentery: A New Approach to Treatment, Lancet **2**: 68-82, 1945.
2. McVay, L. V., Jr.; Laird, R. L., and Sprunt, D. H.: Treatment of Amebiasis with Aureomycin, South. M. J. **43**: 308-313, 1950.
3. Armstrong, T. G.; Wilmot, A. J., and Elsdon-Dew, R.: Aureomycin and Amœbic Dysentery, Lancet **2**: 10-12, 1950.
4. Most, H., and Van Assendelft, F.: Laboratory and Clinical Observations on Effect of Terramycin in the Treatment of Amebiasis, Am. J. Trop Med. **31**: 284-285, 1951.
5. Tobie, J. E.; Most, H.; Reardon, L., and Bozicevich, J.: Laboratory Results on the Efficacy of Terramycin, Aureomycin and Bacitracin in the Treatment of Asymptomatic Amebiasis, Am. J. Trop. Med. **31**: 414-419, 1951.
6. Killough, J. H., and Magill, G. B.: Terramycin in Epidemic Typhus, Amebic Dysentery and Typhoid, J. A. M. A. **147**: 1737-1740 (Dec. 29) 1951.

revealed various degrees of mucosal ulceration, inflammation, and edema. The loading dose of oxytetracycline was 50 mg. per kilogram of body weight given in the first hour. The dose administered for the first three days was 150 mg. per kilogram per day, after which it was reduced to 75 mg. per kilogram per day for the remainder of the treatment period of 14 days. In all patients there was disappearance of bloody diarrhea, tenesmus, and other dysenteric symptoms within two to six days. Stools and proctoscopic specimens became negative for amebas after two days in four patients and after eight days in the remaining patients. In one patient a hepatic abscess developed during oxytetracycline therapy.

CHARACTERISTICS OF TREATED PATIENTS

The patients considered here were among those with diarrheal disease, which included both bacillary and amebic dysentery, who were referred for hospitalization by the physicians in the compound dispensaries. The criteria for acceptance in the amebic dysentery study series were the presence of diarrheal disease with mucosanguineous exudate in the stools, visualized enteric lesions, and the presence of trophozoites of E. histolytica. No patient in this series was asymptomatic with only cysts of E. histolytica in the feces. The following case is representative of those in the series.

TABLE 1.—*Clinical Data in 644 Cases of Acute Amebic Dysentery*

Observations	No. of Cases	Percentage
Onset		
Sudden	134	21
Gradual	460	71
Chief Complaint		
Abdominal pain and/or diarrhea	630	98
Clinical Findings		
Abdominal pain	596	92
Tenesmus	585	91
Borborygmus	290	45
Anorexia	241	37
Feverishness	172	27
Nausea and/or vomiting	82	13
Mucus and/or blood in stool	626	97
Abdominal tenderness	550	85
Temperature of 100 F or above	165	26
Hepatomegaly	115	18
Dehydration	64	10
Sigmoidoscopic observations *		
Ulcers	489	87
Hyperemia	329	59
Edema	279	50

* Sigmoidoscopy was done in only 560 cases, and the percentages for sigmoidoscopic observations are of this number and not the total number of cases.

A 24-year-old Korean was admitted to the hospital in July, 1951. He reported no previous bloody diarrhea. Ten days before admission he began to have mild, bilateral, low abdominal pain and an increase in stools from his normal of one to three per day. Pain persisted and became severer. Five days before admission he had onset of tenesmus and noted for the first time bright red blood and some mucus in his stool. On admission to the hospital his temperature was 98.6 F, he was well nourished and well hydrated, and did not appear ill. The abdomen was soft, but the patient guarded both lower quadrants and there was moderate bilateral low abdominal tenderness without rebound pain. On his first hospital day, he had five soft stools covered with bright red exudate; microscopically there were numerous red blood cells and many motile trophozoites of E. histolytica. Sigmoidoscopic examination revealed 20 to 30 discrete, deep ulcers in the rectum, but the intervening mucosa otherwise appeared normal. Material aspirated from one of the ulcers was teeming with trophozoites of E. histolytica.

A summary of the clinical data in all cases of amebic dysentery in which the patients were admitted to the hospital, including 106 not in the treatment series, is given in table 1. Commonly the onset was gradual. Most of the patients were admitted because of bloody diarrhea that was ordinarily associated with abdominal pain and tenesmus. Other symptoms shown in the table occurred less frequently. The commonest physical finding was abdominal tenderness, which was usually confined to the lower quadrants and at times only to the area over the cecum. About one-fourth of the patients had fever. A slight enlargement of the liver was found in 18% of the patients, and in 6% there was tenderness on palpation. Later in the study, liver abscess, diagnosed on clinical evidence and considered to be amebic, was encountered in four cases and amebic hepatitis was diagnosed in six cases. Hepatomegaly was found twice as frequently in patients with amebic dysentery as in those with bacillary dysentery. Another contrast with bacillary dysentery was the fact that very few of the amebic dysentery patients showed gross evidence of fluid and electrolyte loss.

Ulceration of the rectal mucosa, the most frequent sigmoidoscopic finding, was seen in 87% of all patients examined. Mucosal edema and hyperemia were the other

TABLE 2.—*Drugs and Dosage Schedules Used in 538 Cases of Acute Amebic Dysentery*

Treatment Agent	Dosage
Standard Amebacides	
1. Emetine	0.03 gm. twice a day for 4 days
2. Carbarsone	0.25 gm. three times a day for 7 days
3. Chiniofon	1.0 gm. three times a day for 7 days
4. Chloroquine base	0.3 gm. twice a day for 2 days or more 0.3 gm. three times a day for 19 days
5. Emetine, carbarsone, and chiniofon, given concurrently	0.03 gm. twice a day for 4 days 0.25 gm. three times a day for 7 days 1.0 gm. three times a day for 7 days
6. Bismuth glycolylarsanilate and chloroquine diphosphate	0.5 gm. three times a day for 7 days 0.15 gm. three times a day for 7 days
Antibiotics	
7. Oxytetracycline	a. 2 gm. initially, 0.5 gm. every 6 hr. for 10 days b. 2 gm. initially, 0.5 gm. three times a day for 10 days c. 2 gm. initially, 0.5 gm. every 6 hr. for 5 days
8. Aureomycin	2 gm. initially, 0.5 gm. every 6 hr. for 10 days
9. Chloramphenicol	2 gm. initially, 0.5 gm. every 6 hr. for 10 days
Antibiotics and Amebacides Combined	
10. Oxytetracycline with	2 gm. initially, 0.5 gm. three times a day for 10 days
a. Emetine	0.03 gm. twice a day for 4 days
b. Carbarsone	0.25 gm. three times a day for 7 days
c. Chiniofon	1.0 gm. three times a day for 7 days
d. Bismuth glycolylarsanilate and chloroquine diphosphate	0.5 gm. three times a day for 7 days 0.15 gm. three times a day for 7 days
e. Chloroquine	0.3 gm. twice a day for 2 days; 0.3 gm. per day for 5 days
11. Oxytetracycline with	2 gm. initially, 0.5 gm. every 6 hr. for 5 days
chloroquine	0.3 gm. twice a day for 2 days; 0.3 gm. per day for 3 days
12. Aureomycin with	2 gm. initially, 0.5 gm. every 6 hr. for 10 days
chloroquine	0.3 gm. twice a day for 2 days; 0.3 gm. per day for 5 days
Supportive Therapy	Bed rest and nutritional supplements

conditions observed oftenest (table 1). The typical amebic ulcer was small and discrete, with a thin gray-white exudate. Ordinarily the mucosa between the ulcers appeared relatively normal. The number of ulcers was often unexpectedly large; many patients had as many as 100 varying in size and depth in the terminal 4 cm. of the rectum. This intestinal ulceration contrasted impressively with the good general condition and mild symptoms of the patients. Microscopic examination of material aspirated from these ulcers showed large numbers of actively motile E. histolytica trophozoites, which were usually engorged with red blood cells. Cellular exudate was scant, with red blood cells most common and pus cells rare.

STUDY PROCEDURES

Diagnostic observations in addition to detailed history and physical examination included bacteriological cultures and microscopic examination of feces. There was also a sigmoidoscopic examination with a repetition of the bacteriological and microscopic studies of exudate collected from the most abnormal area. Patients with a diagnosis of amebic dysentery who satisfied the criteria for admission to the series were transferred to the special ward for patients to be studied and assigned in rotation to a predetermined treatment schedule.

Patients with amebic dysentery were followed for six weeks from the beginning of therapy. Saline smears of stool specimens were examined for E. histolytica on the first, second, fourth, and sixth days and once a week thereafter. Before discharge, three specimens were collected after a saline purge and examined microscopically. During the last three months of the study an examination by the zinc sulfate centrifugal flotation method was done at two weeks, five weeks, and six weeks after onset of therapy. The sigmoidoscopic examination with associated bacteriological and parasitological tests was repeated once a week. The criteria of cure were no diarrhea, no exudate in the stools, no E. histolytica trophozoites or cysts, no sigmoidoscopic evidence of colitis, and freedom from significant symptoms of enteric disorder. Treatment was recorded as successful when the patient improved with therapy and remained well and free of E. histolytica for the six weeks of observation. Treatment failures varied in degree from no significant improvement to a favorable clinical and parasitolological response but with a return of E. histolytica before the end of the period of observation.

Treatment was provided in accordance with the predetermined schedules shown in table 2. All were not in operation concurrently, but two groups continued through the entire study. As there was no suggestion of any variation in the clinical severity or character of the disease during the eight months of the study, the findings will be presented and discussed in the order shown in the table.

All patients were followed on the wards by Korean aids and physicians as well as by American corpsmen and physicians. The clinical judgment of the responsible physician dictated any change in the predetermined therapeutic schedules. Very few treatment changes were made with less than two weeks' observation.

TABLE 3.—*Therapeutic Response in 538 Cases of Acute Amebic Dysentery Assessed at End of Six Weeks*

Treatment Agent	No. of Cases	Therapeutic Response		Number Re-treated Before 6 Wk.	Failures Followed for 6 Wk.		
		Success	Failure		Number with E. Histolytica in Stools at 6 Wk.	Number Clinically Ill	Number with Active Colitis Sigmoidoscopically
Standard Amebacides							
Emetine	22	10	12	2	10	1	1
Carbarsone	22	4	18	12	6	2	3
Chiniofon	24	9	15	6	9	1	1
Chloroquine	31	13	18	5	13	6	5
Emetine, carbarsone, and chiniofon	23	19	4	0	4	0	0
Bismuth glycolylarsanilate and chloroquine diphosphate	22	11	11	4	7	3	0
Antibiotics							
Oxytetracycline	104	98	6	3	3	2	3
Aureomycin	41	31	10	3	7	4	2
Chloramphenicol	41	11	30	9	21	10	13
Antibiotics and Amebacides Combined							
Oxytetracycline and standard amebacides for 10 days	97	93	4	2	2	1	1
Oxytetracycline and chloroquine for 5 days	22	20	2	1	1	1	1
Aureomycin and chloroquine for 10 days	23	23	0	0	0	0	0
Supportive Therapy							
Bed rest and nutritional supplements	66	11	55	39	16	8	11

RESULTS

The therapeutic response as assessed at the end of six weeks in 538 cases of amebic dysentery is shown in table 3. Standard amebacides used individually were inadequate therapeutic agents in this group of cases. Patients treated with emetine responded symptomatically, and only 2 of the 22 patients required re-treatment before the end of the follow-up period. However, 10 others had E. histolytica in the stool at the end of six weeks, and one of these had a recurrence of clinical symptoms. Carbarsone and chiniofon treatment resulted in 33 failures as compared with 13 successes. There were 18 failures in the 31 cases in which chloroquine was used.

Combinations of standard amebacides proved to be much more effective in the treatment of acute amebic dysentery. In 23 cases a combination of emetine, carbarsone, and chiniofon was given. All of these patients had good initial clinical responses. None had recurrence of

clinical symptoms, but four had reappearance of E. histolytica in the stools at the end of six weeks.

The combination of bismuth glycolylarsanilate and chloroquine diphosphate [7] gave a satisfactory early clinical response in 18 of 22 cases. In addition to the four cases with clinical failures, in seven others E. histolytica reappeared in the stools, in three with a recurrence of symptoms.

Oxytetracycline proved to be the most effective of the antibiotics. A total of 104 patients were treated with this drug in varying dosage, and all responded clinically. Six relapsed, however, three early in the follow-up period, and three later. One of these six had clinical amebic hepatitis. The remaining 98 were well and free of evidence of recurrent infection at the end of six weeks. Aureomycin also produced a good initial response in all but 3 of the 41 cases. At six weeks 7 of the remaining 38 patients had E. histolytica in the stools, and 4 of these had symptoms. Chloramphenicol proved to be ineffective in this disease. Only 11 of 41 patients treated responded satisfactorily, and most of the patients who were treatment failures had E. histolytica in their stools until they were re-treated with another drug.

Oxytetracycline was given in combination with the five standard amebacides listed. These combinations were effective therapeutics, since in 97 cases there were only 4 failures, 3 with a recurrence of symptoms. In no instance was there more than one failure in any of the five treatment groups. When oxytetracycline and chloroquine were given for only five days, 2 of the 22 patients relapsed. There were no failures in 23 cases in which aureomycin and chloroquine were given.

There were 66 patients followed without specific therapy. Of this group, 39 were assigned to a specific treatment schedule before the end of six weeks. At the termination of the follow-up period 11 of the 66 patients had no clinical or parasitological evidence of amebic infection. These patients by the standards used would be counted as successfully treated, and in addition five others with stools still positive for E. histolytica had recovered clinically. These observations show that spontaneous recovery does occur and must be given consideration in the evaluation of any specific therapy.

A group of 16 patients successfully treated with antibiotics combined with other amebacides were followed in greater detail early in the period of therapy to determine the rapidity with which ulcers had healed and amebae had disappeared from lesions. Patients were examined sigmoidoscopically daily. Material was aspirated from ulcers and subjected to a prolonged search for E. histolytica. The average time required in these 16 cases for E. histolytica to disappear from lesions was 48 hours, the minimum being 36 and the maximum 72. Hyperemia and mucus exudate decreased within 18 hours, as did the white exudate covering most amebic ulcers. Within 48 to 72 hours, epitheliazation had begun. Many discrete, shallow ulcers healed in 72 to 96 hours, with only slight hyperemia of the mucosa at the site of the previous ulcer. The large, deep, confluent lesions healed more slowly by granulation of bases; these lesions usually left some residual scarring and dimpling of the mucosa.

We noted that microscopic examination of stools or aspirated exudate gave earlier and more accurate evidence of recurrence than did sigmoidoscopic observation or clinical examination. Patients usually had evidence of E. histolytica before symptoms or rectal lesions developed. This was illustrated in the 68 patients treated with either emetine, carbarsone, or chiniofon. Twenty-five of these patients had E. histolytica in their stools at the time of the six week examination; however, only four had symptoms and one other had sigmoidoscopic evidence of recurrent colitis.

SIDE REACTIONS TO THE ANTIBIOTICS

There were surprisingly few gastrointestinal side reactions to the antibiotics among this group of persons. Occasionally nausea was reported when aureomycin was given for 10 days. No pruritis ani or evidence of proctitis was encountered following the use of oxytetracycline, nor was diarrhea a recognized problem following administration of this drug. These observations are to be interpreted with caution, since the patients spoke a different language and had eating and living habits that differ considerably from ours.

COMMENT

It has been pointed out that all patients in this series were ill, and compared with the sporadically occurring disease in the United States, they would be considered to have severe disease. Fulminating infections suggesting an acute surgical condition in the abdomen were not seen, in contrast with the observations in the Chicago epidemic of 1933. Bacillary and amebic dysentery were being studied and treated simultaneously, and we were impressed by the frequency with which these two diseases presented different clinical pictures. The relative appearance of well-being of the amebic patients, even those whose sigmoidoscopic examination revealed extensive enteric lesions, was in marked contrast to that of the acutely ill, toxic, dehydrated patients with shigellosis.

The circumstances under which this study was conducted restricted the duration of the post-treatment follow-up. It was practicable to retain patients in a hospital convalescent ward up to six weeks after the beginning of therapy. Here the treated patients could be observed in an environment relatively free of infection and under continuous and close medical supervision. On discharge the patients became a part of a population with a high infection rate. Later reexamination would not have differentiated possible recurrence from probable reinfection. Hence follow-up was terminated with discharge from the hospital.

Complications in one patient treated with antibiotics call attention to a possible limitation of this therapy. During a successful treatment with oxytetracycline of the enteric manifestations of the disease, a septic temperature and leukocytosis developed and the patient's liver progressively increased in size and became tender. These symptoms subsided following therapy with chloroquine. Killough and Magill [6] report a case in which a liver abscess developed during treatment with oxytetracycline. The advisability of combining antibiotic and chloroquine therapy therefore calls for careful consideration. The

7. This combination of drugs was supplied to us for a specific trial as a prophylactic agent. Conditions were such that our information on prophylactic therapy is incomplete.

findings suggest an advantage of combined therapy, but further observations are needed since our data indicate that there are inadequacies even in the best therapy now available.

CONCLUSIONS

The value of emetine, carbarsone, chiniofon, bismuth glycolylarsanilate (milibis®), chloroquine, oxytetracycline ("terramycin"), aureomycin, and chloramphenicol was compared in a series of 538 cases of acute amebic dysentery. Carbarsone, chiniofon, chloroquine, and chloramphenicol used alone had minimal therapeutic value in this disease. Emetine and aureomycin alone and the combination of bismuth glycolylarsanilate and chloroquine diphosphate (milibis®-aralen®) gave a good initial response but a high relapse rate. Emetine, carbarsone, and chiniofon combined gave an excellent initial response and a moderate relapse rate. Oxytetracycline alone and in combination with (1) emetine, (2) carbarsone, (3) chiniofon, and (4) chloroquine diphosphate, (5) bismuth glycolylarsanilate and chloroquine and the combination of aureomycin and chloroquine diphosphate all gave excellent initial responses and the lowest relapse rates observed. Additional studies of the more promising treatment schedules are advisable.

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EVALUATION OF THE NEWER AMEBACIDES

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In recent years both the research worker and the practicing physician have become increasingly aware of amebiasis both as a disability for the patient and as a menace to public health. In part this trend is due to an understanding of the manifold manifestations of the disease, but primarily interest has been stimulated by the availability of a series of new drugs with amebacidal properties.

Among the antibiotics, aureomycin, chloramphenicol (chloromycetin®), and oxytetracycline ("terramycin") have all been studied at some length. Long known as an effective antimalarial agent, chloroquine has been pronounced by Conan [1] to be of decided value in amebic hepatitis. The work of other investigators, including Basnuevo and Estarlí of Cuba,[2] Fournier Villado and Treviño Villaseñor of Mexico,[3] and Emmett of Chicago,[4] has confirmed its usefulness. More recently bismuth glycolylarsanilate (milibis®) has gained considerable standing, especially among physicians of Latin America, in the treatment of intestinal amebiasis.

The availability of so many new drugs in so short a period of time has made their comparative evaluation extremely difficult. Even under ordinary circumstances, it is no small task to gather together a large enough group of patients for the study of a single amebacide. To keep the group together for control examinations long enough to distinguish the permanent eradication of the trophozoites and their cysts from their temporary disappearance is even more difficult.

The present study involves 264 cases of amebiasis with follow-up physical and stool examinations ranging from a minimum of 6 to a maximum of 24 months. In order to evaluate the effectiveness of the amebacides under discussion, this series is broken down into eight treatment groups: those treated with bismuth glycolylarsanilate, aureomycin, aureomycin and bismuth glycolylarsanilate, chloramphenicol, chloramphenicol and bismuth glycolylarsanilate, oxytetracycline alone, oxytetracycline and bismuth glycolylarsanilate, and chloroquine and bismuth glycolylarsanilate.

Although the basic purpose of this paper is to evaluate these several drugs, alone and in combination, the large number of cases observed and the long period during which the study was carried out—work was begun in April, 1950—have made it necessary to consider associated problems as well. Thus, during the course of this study, I have come to the conclusion that the incidence of amebiasis is much greater than the general practitioner, even in subtropical regions, is likely to suspect. In Caracas, Venezuela, with temperature ranges and rainfall quite comparable to those of many southern cities of the United States, the middle and upper income groups show an incidence of at least 8.9%. It would be difficult to overestimate the incidence among the masses of underprivileged who live unhygienically crowded together in the capital city.

I have also observed that amebiasis is basically a systemic disease. Even in the early stages of its development it is unwise to base its treatment on the textbook concept of intestinal as distinct from extraintestinal amebiasis. The most effective treatment of amebiasis requires the use of both an absorbable and a nonabsorbable amebacide. Neither the one nor the other gives maximum results when employed alone. In the present study the treatment of preference is administration of a combination of bismuth glycolylarsanilate and chloroquine or of bismuth glycolylarsanilate and oxytetracycline.

PREVALENCE OF AMEBIASIS

Over a period of five years approximately one out of every three patients arriving at my office for treatment proved to be carrying either trophozoites or cysts of Endamoeba histolytica. A careful stool examination became routine for all patients, independently of the symptoms described.

Also the incidence of asymptomatic carriers is very high. In April, 1951, through the cooperation of the parents, teachers, and students of the American High

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1. Conan, N. J., Jr.: Chloroquine in Amebiasis, Am. J. Trop. Med. **28**: 107-110 (Jan.) 1948.

2. Basnuevo, J. G., and Estarlí, E. G.: Absceso Hepático Amibiano Carado con Cloroquine, Rev. Kuba Med. trop. **5**: 31-37 (March-April) 1949.

3. Fournier Villado, R., and Treviño Villaseñor, A.: La Cloroquina en el Tratamiento del Absceso Hepático Amibiano, Presna méd. mex. **15** (no. 4): 84-87 (April) 1950.

4. Emmett, J.: Refractory Amebic Abscess of the Liver Treated with Chloroquine, J. A. M. A. **141**: 22-24 (Sept. 3) 1949.

School of Bello Monte, the Christian Brothers of the La Salle Seminary, and the employees of the Sydney Ross Company of Caracas, a mass survey was carried out on the incidence of intestinal parasites. The survey covered whole family groups and involved 1,502 persons.

Because of the large number of people taking part and the necessity of their complete cooperation, the conditions required to obtain results with scientific exactitude could be only approximated. Adults were asked to take as a laxative 4 tbsp. (about 120 cc.) of magnesium hydroxide (milk of magnesia) before retiring, while children were limited to 2 tbsp. (about 60 cc.). Stool specimens were gathered from the second evacuation of the following morning, and the examinations were completed before noon of the same day. Stools negative for trophozoites and cysts on direct examination were concentrated, using the technique of Stoll and Willis.

No doubt the survey would have been more accurate if it had been possible to insist on a stronger purgative and if the specimens had been collected in the laboratory itself for immediate warm stool examination. Nevertheless, the results revealed a disquietingly high proportion of parasitism. The findings are summarized in table 1.

TABLE 1.—*Parasites Found in Stools of 1,502 Persons Surveyed*

Type of Parasite	No. Positive	% Positive
E. histolytica	134	8.92
Ameba coli	274	18.24
Other protozoa	10	0.64
Ascaris lumbricoides	171	11.38
Necator Americanus	56	3.73
Oxyuris	5	0.34
Tricocephalus	155	10.99
Other nonprotozoan	1	0.07
Total positive	688	45.81
Total negative	814	54.19
Totals	1,502	100.00

All participants were well above average in educational background. All belonged to groups higher than average in the economic and social scales. The limitations of the collection and examination techniques resulted in many specimens being overlooked that under better conditions might have proved positive for trophozoites of E. histolytica. With these factors in mind, it is certainly safe to say that no less than 10% and possible as high as 25% of the population of Caracas are either carriers of, or suffer from, some form of amebiasis.

While many other observers have reported incidences of over 10% in the United States,[5] very little survey work has been done in Venezuela; and in the case of Caracas, previous reports have indicated an incidence considerably lower than the 8.92% shown by this study. Thus, Gabaldón reported 6.8%, while Briceño Rossi's work revealed an incidence of only 6%.[6] The lack of adequate statistical data makes further investigation a necessity if amebiasis is to be appreciated in its true importance.

5. Craig, C. F.: The Etiology, Diagnosis, and Treatment of Amebiasis, Baltimore, Williams & Wilkins Company, 1944, pp. 42-43.

6. Galbadón and Rossi, cited by Calvó Fonseca, R.: La Incidencia de la Entamoeba histolytica en Cuba-Bol.; plan para lograr la uniformidad de los métodos de investigación y ténicas de examen coprológico a usar en las encuestas sobre Entamoeba histolytica, en los países americanos, Bol. Ofic. san. panam. **26**: 943-952 (Nov.-Dec.) 1947.

AMEBIASIS AS A SYSTEMIC DISEASE

The claim that amebiasis should be considered a systemic disease, that is, a disease with both intestinal and extraintestinal involvement, usually of the liver, and treated as such is based on evidence that may be considered conveniently from four standpoints: (1) the great variety of subjective symptoms reported by the patients covered by this study; (2) laboratory findings such as high icterus index, accelerated sedimentation rate, leukocytosis, and elevated levels of serum bilirubin and alkaline phosphatase, which indicate periportal inflammation and fibrosis of the liver; (3) failure of the patients to respond uniformly to bismuth glycolylarsanilate, a highly nonabsorbable arsenical of great amebacidal power; and (4) satisfactory response of these patients when bismuth glycolylarsanilate was combined with an effective absorbable amebacide.

The impracticability of dividing amebiasis into the extraintestinal and intestinal forms was dramatically demonstrated in May, 1950. During the first days of that month 27 patients came to my office with surprisingly similar histories and complaints. All of these patients had been indulging heavily in alcohol during the days preceding a national holiday. Their symptoms were much the same; they had brief chills, temperature varying between 99 and 101 F, sweating at night, painful liver, with radiation of pain from the right side to the back and shoulder, accentuated by movement, pressure, and inspiration, nausea, vomiting, and constipation. These patients were also subject to coughing spells, which, in several instances, they attributed to heavy smoking.

The laboratory reports revealed the following blood observations: a white cell count of more than 10,000, with neutrophilia, high sedimentation rates, and an icterus index ranging between 12 and 22 units. There was no anemia. Examination of initial warm stool specimens taken from the second evacuation after a strong purgative revealed 19 cases of E. histolytica, with the trophozoites between 16 and 25 μ in size. A second examination four days later revealed trophozoites in seven additional cases, while quadrinucleate cysts of E. histolytica were revealed in the remaining case.

Since amebiasis is seldom limited to one member of a family and since to reduce the possibilities of reinfection within the group it is always wise to treat all infected members simultaneously, the families of the original 27 patients were checked, and 74 additional cases were discovered. Fifteen families had from three to seven members infected.

The symptoms reported in the new cases correspond in almost every way with those of the first set. Seventeen family groups told of an influenza-like infection in the household. Rectoscopic examinations of both groups revealed superficial necrotic flask-shaped ulcers, surrounded in 53 instances by normal mucosa, while the 48 remaining patients showed inflammatory changes. Roentgenograms of the colon in 12 cases revealed a cone-shaped cecum as well as localized spasm of the cecum and colon.

Acute appendicitis developed in three patients during treatment 17, 60, and 87 days after the initial attack. In all three instances the pathological report proved Endamoeba organisms responsible, trophozoites 15 to 25 μ in

size being present. There was multiple perforation of the appendix, with accompanying peritoneal irritation.

In October a second outbreak occurred, and in the space of three weeks 40 patients were confined, which, with 22 additional patients seen between May and October, brought the total in seven months to 167. Subjective and objective symptoms were much the same as in the first outbreak, except that the trophozoites were much smaller, ranging from 8 to 12 μ in size, with cysts of between 4 and 6 μ. Blood examinations revealed hypoglycemia, hypochromic anemia, a high sedimentation rate, and an elevated icterus index. The stools showed impaired digestive function, with starch present in all cases.

In the space of 10 months we were faced with a bewildering variety of symptoms, all due to infestation by E. histolytica. Table 2 summarizes the clinical picture not only for the 167 cases already mentioned but also for the entire group covered by this study. Subjective and objective symptoms, along with pertinent laboratory findings, are included. In all cases cysts or trophozoites or both were found.

E. histolytica trophozoites establish themselves in the wall of the large intestine, especially in the iliocecal region, ascending colon, and rectosigmoid. They penetrate the mucosa and congregate in nests in and along the thrombosed veins and capillaries, eventually gaining access to the liver. No doubt this explains the high percentage of patients shown in table 2 reporting chills and pain in the upper quadrant, and having a high icterus index, high serum phosphatase level, and high serum bilirubin level. A review of the findings listed in table 2 indicates that more than 60% of these patients were suffering from some degree of liver involvement.

TREATMENT OF AMEBIASIS AS A PURELY INTESTINAL INFESTATION

If amebiasis could be considered an intestinal disease, with only infrequent extraintestinal involvement, the ideal treatment agent in the majority of cases should be a drug of high amebacidal power that is relatively insoluble and with minimum absorbability. Topical action in the intestine would thus be combined with low toxicity to produce a nearly ideal amebacide.

The value of arsenical compounds in amebiasis has long been recognized. Recently, a new arsenical, bismuth glycolylarsanilate, has become available in 500 mg. tablets containing 15.01% of pentavalent arsenic and 41.8% of bismuth. Hansen and Dennis [7] and other investigators have proved it to be of high amebacidal activity in solutions of from 1:30,000 to 1:35,000. McChesney and Hoppe [8] administered as much as 10 gm. per kilogram of body weight to hamsters daily for 21 days without producing signs of toxic absorption. Further studies in human beings indicated a maximum urinary elimination of 2% of the arsenic administered.[8] With these data in mind, bismuth glycolylarsanilate was chosen as the amebacide most likely to fulfill requirements for a drug whose effectiveness could reasonably be expected to be limited to topical action in the intestines.

A total of 87 persons were treated with this drug. Basically, the schedule of treatment used was that recommended by D'Antoni in a personal communication to me. For 35 days all patients were requested to take six tablets daily (3 gm.), in three equal doses, preferably after meals. Every fifth day this medication was omitted, and a magnesium sulfate purgative was taken in order to clear the intestines of the endotoxins produced by the destruction of the amebas. In addition to bismuth glycolylarsanilate, an elixir containing hyoscyamine sulfate, atropine sulfate, hyoscine hydrobromide, and phenobarbital (donnatal®) and an ox bile extract (ketochol®) were prescribed, before and after each meal, respectively, to encourage drainage of the liver, common duct, and gallbladder.

Warm stool examinations were made on the 42nd day after beginning of treatment. Thus, seven days were allowed to pass without the administration of any drug, to guarantee complete clearance of arsenical traces from the intestines. As in all other follow-up stool examinations mentioned in this paper, the sample was taken in our laboratory from the second evacuation after a strong purgative of magnesium sulfate. Stools negative on direct examination were concentrated according to the technique of Stoll and Willis, and a second specimen was taken two to four days later in all cases with negative results reported from the first series.

In cases with positive results a second course of treatment was given, and at the end of six weeks these cases plus those with negative results after the first courses were examined once more, using the technique described above. Patients whose stools still contained cysts or trophozoites were given bismuth glycolylarsanilate until they had received a maximum of 400 tablets, or 200 gm. during the entire course of treatment.

TABLE 2.—*Clinical and Laboratory Findings in Cases with E. Histolytica Infestation*

Complaints of Patients	Number	Percentage
Epigastric pains	162	61.36
Weakness and exhaustion	222	84.09
Chills and fever	172	65.15
Right upper quadrant pain	192	72.73
Cough, with fever	110	41.62
Nausea	250	94.70
Diarrhea	190	71.97
Constipation	70	26.52
Clinical Symptoms		
Typhoid-like symptoms and feverishness	114	43.18
Low blood pressure	201	77.15
Temperature 101 to 103 F	170	64.39
Tender liver, extending two fingerbreadths below costal margin	180	68.18
Tender colon, with lower left quadrant pain	142	53.79
Laboratory Findings		
Leukocyte count of 11,000 to 15,000	166	62.88
Erythrocyte count of 3.7 to 4.2 million	189	71.59
Hemoglobin level of 11 to 13 gm. per 100 cc.	240	90.90
Thymol turbidity 2.8 to 6.5 units	192	72.73
Cephalin flocculation 1+ in 48 hr.	194	73.48
Cephalin flocculation 2+ in 48 hr.	49	18.56
High serum bilirubin level	87	32.95
High phosphatase level	91	34.47
High icterus index	199	75.38
Cysts of E. histolytica	260	98.48
Trophozoites of E. histolytica	195	74.87

7. Dennis, E. W.; Berberian, D. A., and Hansen, S. S.: Amoebicidal Activity of Bismuthoxy-p-N-Glycolyl-arsanilate and 7-Iodo-4-(1-Methyl-4-Diethylaminobutylamino) Quinoline Diphosphate, Am. J. Trop. Med., **29**: 683-689 (Sept.) 1949.

8. McChesney, E. W., and Hoppe, J. O.: Absorption, Excretion, and Toxicity of Milibis (Bismuthoxy-p-N-Glycolylarsanilate) Following Oral Administration, Proc. Soc. Exper. Biol. Med., **73**: 326-330 (March) 1950.

Results are summarized on table 3. At the end of six months 45 patients, or 51.7% of the total 87, still had cysts in their stools. This group, plus an additional patient with negative stools at the end of the six months which became positive shortly thereafter, were given aureomycin. All patients whose stools were negative were kept under observation for a two year period from the beginning of treatment.

Although bismuth glycolylarsanilate eliminated all trophozoites by the end of the first 35 day course of treatment, at no time did it eliminate cysts in more than 54% of our cases, and this high point was reached at the end of the three month period. The control examinations at six months revealed five relapses, with stools positive for cysts. I believe that in the cases in which stools were reported as negative at the end of one year the trophozoites and their cysts may be considered as permanently eradicated. The high possibilities of reinfection make it unwise to accept the lower negative figures reported at the 18th month and two year control intervals. Thus, in this series of 87 cases bismuth glycolylarsanilate brought satisfactory results in 46% of the total.

The effectivity of this drug bore no relationship to age, weight, physical condition, sex, or race of the patient. Moreover, there was no appreciable difference in its activity in relation to the two strains of trophozoites and cysts mentioned earlier. The large quantities of pentavalent arsenic administered also make it extremely unlikely that the failures were caused by an arsenic-resistant strain of amebas.

Although other investigators have suggested that a nonabsorbable drug may be ineffective against amebas buried in intestinal cysts beyond its field of action, which responded to an absorbable amebacide carried by the bloodstream, I believe that this concept—while possibly important as a contributing factor—does not offer a complete explanation of the failure of bismuth glycolylarsanilate in 47 cases. Without exception these patients revealed many of the clinical symptoms and laboratory findings presented in table 2 as indicative of liver involvement; and it will be noted that the proportion of cases resistant to bismuth glycolylarsanilate (54%) correlates to a reasonable degree with the 60% of the total 264 cases under study in which some degree of liver involvement was evident. Moreover, in the 47 cases in which stools became negative for cysts after subsequent treatment with absorbable amebacides, clinical symptoms also subsided and the laboratory findings became normal before the patients were released from treatment.

In view of these facts, I ascribe the failure of this drug in more than 54% of the cases primarily to the circumstance that something more than an intestinal infestation was present, and therefore completely successful results could not be expected with a drug limited in its action to the intestines. It would appear that 47 of the 87 patients were suffering from a systemic disease, indicating that extraintestinal involvement is much more frequent than is usually supposed and that the division established between intestinal and extraintestinal forms of amebiasis is largely an academic concept. Further evidence on this point will be offered in a later section dealing with the response of these patients to treatment with an absorbable amebacide.

TABLE 3.—*Response to Various Amebacides* *

Time of Examination	Stools Positive for Cysts: No.	Stools Positive for Cysts: %
Bismuth Glycolylarsanilate (87 patients)		
6 weeks	44	50.6
3 months	40	46.0
6 months	45	51.7
12 months	47	54.0
18 months	55	63.2
2 years	55	63.2
Aureomycin (54 patients)		
Patients Previously Treated (46)		
8 days	40	87.0
16 days	39	84.8
1 month	37	80.4
New Patients (8)		
8 days	6	75.0
16 days	6	75.0
1 month	6	75.0
Bismuth Glycolylarsanilate and Aureomycin (55 patients)†		
Patients Previously Treated (43)		
16 days	39	90.7
1 month	38	88.4
New Patients (12)		
16 days	9	75.0
1 month	6	50.0
Chloramphenicol (22 patients)		
Patients Previously Treated (6)		
1 week	6	100.0
2 weeks	6	100.0
1 month	6	100.0
6 weeks	6	100.0
3 months‡	6	100.0
New Patients (16)		
1 week	13	81.3
2 weeks	12	75.0
1 month	14	87.5
6 weeks	14	87.5
3 months§	14	87.5
Chloramphenicol and Bismuth Glycolylarsanilate (58 patients)		
Patients Previously Treated (44)		
2 weeks	42	95.5
4 weeks	40	90.9
6 weeks	44	100.0
3 months	44	100.0
6 months‡	44	100.0
Patients Previously Treated with Chloramphenicol (14)		
2 weeks	9	64.3
4 weeks	6	42.9
6 weeks	6	42.9
3 months	8	57.1
6 months‡	8	57.1
Oxytetracycline (39 patients)		
8 days	26	....
16 days	23	....
6 months	23	....
Oxytetracycline and Bismuth Glycolylarsanilate (97 patients)		
15 days	61	62.9
30 days	30	30.9
78 days	22	22.7
6 months	22	22.7
Bismuth Glycolylarsanilate and Chloroquine (102 patients)		
Group 1 (60 New Patients and 22 Patients Previously Treated)		
7 days	69	84.1
2 weeks	14	17.1
Group 2 (20 New Patients)		
2 weeks	16	80.0
All Patients Treated with Bismuth Glycolylarsanilate and Chloroquine (102)		
6 months	11	10.8

* The numbers in parentheses indicate the number of patients in each group.

† The stools in all cases became negative for trophozoites.

‡ The stools of all six patients still contained cysts at the end of three months, and the patients were transferred to the group to be treated with chloramphenicol and bismuth glycolylarsanilate.

§ These 14 patients were transferred to the group to be treated with chloramphenicol and bismuth glycolylarsanilate.

‡ At the end of six months these patients were transferred to the group to be treated with oxytetracycline and bismuth glycolylarsanilate.

It is well to point out that this work with bismuth glycolylarsanilate brought ample evidence of its low toxicity and relative nonabsorbability. Only 2 of the 87 patients treated complained of headache while transitory urticaria developed in 2 during the first week. These were the only signs of toxicity, indicating some, though slight, absorption. Sixteen patients complained of pruritus ani, 26 of flatulence, and 28 of indigestion. Of these complaints only the pruritus ani can be ascribed definitely to the topical action of the arsenical. The remaining two are often symptomatic of amebiasis itself, and may not have been caused by the treatment. These results are particularly interesting in view of the large quantities of the drug administered. No patient received less than 84 gm., while four tolerated a total of 200 gm. without difficulty.

AUREOMYCIN ALONE AND IN COMBINATION WITH BISMUTH GLYCOLYLARSANILATE

When this study was initiated, reports on the value of aureomycin, while not conclusive, did indicate that the drug might prove of real importance in this field. Since that time, however, further studies have assigned it a far less important role than was originally expected. In view of the great amount of work done by other investigators, I did not feel justified in including as large a group of patients for treatment with aureomycin alone as with bismuth glycolylarsanilate. Nevertheless, the 46 patients who failed to respond to the arsenical and 8 new patients with both cysts and trophozoites in their stools were treated for periods up to one month with aureomycin alone. The results, as shown on table 3, were far from encouraging, and corroborated the findings of previous studies.

As in the work with bismuth glycolylarsanilate, our treatment schedule was a simple one: a total of six 250 mg. capsules of aureomycin daily, accompanied by vitamin B complex and B_1 both orally and parenterally to reduce the incidence of side-effects, were given for eight days. No more than four eight-day courses were administered.

Stool examinations were made at the end of each treatment schedule. At the end of the first course trophozoites had disappeared from the feces of the eight new patients, but only two had no cysts. At the end of one month a total of 11 patients had stools negative for both cysts and trophozoites, remaining negative for six months after the beginning of treatment. They may therefore be considered as permanently freed from the infestation, so that treatment with aureomycin was effective in 20.4% of cases. This is considerably less effective than bismuth glycolylarsanilate after a control period of 12 months.

In contrast to the excellent tolerance to bismuth glycolylarsanilate alone, these patients reacted poorly to aureomycin. During the first week, the following symptoms of intolerance were shown: pruritus ani in 46 cases, indigestion or colic in 39 cases, urticaria in 13 cases, and glossitis in 27 cases. During the fourth course of treatment a severe urticarial reaction developed in six patients, with temperatures ranging between 102 and 103 F. Fortunately, the urticaria cleared rapidly in all 19 cases in which it occurred when diphenhydramine (benadryl®) hydrochloride was administered in 50 mg. capsules every four hours for three days.

In summary, in the group of patients treated with aureomycin the drug relieved acute symptoms of amebiasis, destroying the trophozoites, but appeared to have little effect on the resistant cysts, and the results of the extended treatment do not justify the expense involved for the individual. Although aureomycin was unsatisfactory when administered alone, it was felt that before turning to another drug it would be well to ascertain its effectiveness when combined with bismuth glycolylarsanilate. The 43 patients who still had cysts and 12 new patients were therefore given a course of bismuth glycolylarsanilate and aureomycin, making a total of 55 cases.

The schedule of treatment was the same as for aureomycin alone, with the addition of three tablets of 500 mg. of bismuth glycolylarsanilate daily for an eight day period. Results as shown in table 3 confirmed the ability of aureomycin to destroy the trophozoites; but the final picture insofar as permanent eradication of the cysts themselves is concerned was no better than with bismuth glycolylarsanilate alone.

It now proved impossible to continue the study of bismuth glycolylarsanilate and aureomycin in combination, as the 38 patients who still had cysts from the group of 43 could not cooperate further because of the disagreeable, though not dangerous, side-effects produced by aureomycin. The full group of 44 patients that still had cysts was therefore assigned to further therapy with chloramphenicol.

CHLORAMPHENICOL ALONE AND IN COMBINATION WITH BISMUTH GLYCOLYLARSANILATE

Only six patients who had previously been treated with bismuth glycolylarsanilate, aureomycin, or a combination of the two drugs were included in the group to receive chloramphenicol alone. Sixteen new patients, all with stools positive initially for both cysts and trophozoites, completed a total of 22. All patients were given 1.5 gm. of chloramphenicol daily (250 mg. every six hours) for eight days. Stool examinations were made at the end of the 1st, 2nd, 4th, 6th, and 12th week. No one, however, was given more than three eight-day courses of chloramphenicol. Results are summarized in table 3.

At the end of the three month control period only 2 of the 16 new patients had neither trophozoites nor cysts in their stools, and treatment was abandoned shortly thereafter. Thus, no more than 12.5% of the new group can be considered as probably freed of the infestation. Chloramphenicol alone, therefore, was completely ineffective against the cysts in those patients who had received treatment previously. As far as this study is concerned, it was of little value in the elimination of cysts of E. histolytica but was effective against the trophozoites in 100% of the cases. In this respect results paralleled those obtained with aureomycin, but they were superior in the sense that no toxic effects were noted and all patients reported a sense of well-being, with a disappearance of their subjective complaints, during the second week of treatment. It should be added that in 34 patients treated with chloramphenicol the blood cell count showed a hypochromic anemia.

The combined course of chloramphenicol and bismuth glycolylarsanilate was administered to a total of 58 patients, as follows: to 38 who had previously been treated

with bismuth glycolylarsanilate, aureomycin, and a combination of both; to 6 previously treated with the combination plus chloramphenicol; and to 14 previously treated with chloramphenicol alone.

Treatment was continued with 1.5 gm. of chloramphenicol daily, to which was added three tablets of bismuth glycolylarsanilate (1.5 gm.) for an eight day period. No more than three eight-day courses were given to this group, with the response shown in table 3. The figures show that neither aureomycin nor chloramphenicol are of practical significance in the cure of amebiasis, although they may be useful in eliminating the trophozoites and the subjective complaints of the patients.

OXYTETRACYCLINE ALONE AND IN COMBINATION WITH BISMUTH GLYCOLYLARSANILATE

Shortly after its introduction, preliminary studies of oxytetracycline indicated that the new drug might be definitely important as an amebacide, and, at the same time, comparatively free of disturbing side-effects. Unlike bismuth glycolylarsanilate, oxytetracycline is highly absorbable and therefore might be expected to give favorable results in systemic amebiasis.

Oxytetracycline was given to 39 new patients with amebiasis, all with stools positive for both trophozoites and cysts, for a maximum of two eight-day courses. A total of 1.5 gm. was administered daily. Stool examinations were made at the end of each eight day period, and those patients with stools reported negative at 16 days were followed up for a minimum of six months, as shown in table 3.

A single eight day course of oxytetracycline eliminated trophozoites in all cases; and after a second course, in 16 out of 39 cases stools were negative for both cysts and trophozoites, remaining so through the six month control examination. Until the full 12 month period of control has been reached in all cases, there will be some doubt as to whether or not the elimination of the parasites should be considered definitely proved. The majority of patients, however, have been under observation for more than nine months and remain free. It is therefore suggested that these 16 patients (41%) can reasonably be considered as cleared of parasites.

Results with oxytetracycline were most encouraging, nearly equalling those obtained with bismuth glycolylarsanilate alone, which had eradicated cysts and trophozoites in 46% of the patients at the 12 month control period. Unfortunately, the drug had two major drawbacks: its high cost and bothersome side-effects. All 23 patients who still had cysts after two eight-day courses complained of diarrhea, pruritus ani, abdominal cramps, and general malaise. Treatment with oxytetracycline alone was therefore discontinued for 15 days, during which these patients received a course of bismuth glycolylarsanilate followed once more by a course of oxytetracycline.

Inasmuch as oxytetracycline had proved to be the most effective of the absorbable amebacides under study while bismuth glycolylarsanilate had been the drug of choice among the nonabsorbable arsenicals, I was particularly anxious to give the combined treatment to as large a group as possible. In all, a total of 97 patients were included, broken down in this manner: 52 who had been previously treated with chloramphenicol, aureomycin, or bismuth glycolylarsanilate, 23 previously treated with oxytetracycline alone; and 22 new patients.

A somewhat complicated schedule of treatment was set up, in the hope of minimizing the side-effects noted previously with oxytetracycline: six tablets of 500 mg. of bismuth glycolylarsanilate daily for 15 days; 1.5 gm. of oxytetracycline daily for 4 days; 1 gm. of oxytetracycline daily for 11 days; six tablets of 500 mg. of bismuth glycolylarsanilate daily for 30 days; 1.5 gm. of oxytetracycline daily for 8 days; and 1 gm. of oxytetracycline daily for 8 days. The total course, therefore, involved 76 days, but patients with negative stools at 15 and 30 days were dropped from further treatment and continued under observation. The results are summarized in table 3.

In spite of the fact that this group of 97 patients included 52 previously treated with chloramphenicol, aureomycin, or bismuth glycolylarsanilate, the response to the combined course of bismuth glycolylarsanilate oxytetracycline was far superior to anything previously encountered in this study. After the first 30 day course, the stools of 67 patients, or 69.1%, remained negative during the six month control period. The stools of 8 of the remaining 30 became negative after a second, more prolonged, treatment, giving a final result of 75 patients (77.3%) with stools negative for both cysts and trophozoites at the six month control examination.

Thus, the combination of a nonabsorbable and an absorbable amebacide—each of which had previously shown high amebacidal activity when employed alone—proved to be the most effective attack on amebiasis encountered up to this point. From the viewpoint of the practicing physician, therefore, there seems little doubt that amebiasis should be considered a systemic disease rather than a purely intestinal or extraintestinal infection.

COMBINATION OF BISMUTH GLYCOLYLARSANILATE AND CHLOROQUINE

The interest aroused in chloroquine in the treatment of amebic hepatitis by the studies of Conan and others encouraged us to investigate the possibilities of bismuth glycolylarsanilate and chloroquine in combination. Earlier studies had included chloroquine in relatively advanced cases of extraintestinal involvement, with hepatic or pulmonary abscesses, and had required the administration of relatively large quantities of chloroquine, producing a variety of disagreeable side-effects generally necessitating bed rest for the patient. In contrast, it was proposed to employ limited doses of chloroquine in ambulatory patients in no way different from those already mentioned in this study; these patients reported the variety of symptoms mentioned in an earlier section of this paper, but without pronounced hepatic or other extraintestinal involvement.

Winthrop Products, Inc., supplied the two types of experimental bismuth glycolylarsanilate and chloroquine diphosphate (milibis®-aralen®) tablets that were used. The first contained 500 mg. of bismuth glycolylarsanilate and 150 mg. of chloroquine diphosphate, while the second was made up of 400 mg. of bismuth glycolylarsanilate and 100 mg. of choroquine diphosphate.

Eighty new patients with amebiasis and 22 who had received oxytetracycline and bismuth glycolylarsanilate made up a total of 102 patients treated with bismuth glycolylarsanilate and chloroquine. These in turn were divided into two groups: group 1 consisted of 82 patients, including the 22 previously treated with bismuth glycolylarsanilate and oxytetracycline; group 2 consisted of 20 new patients. Group 1 received two tablets (500 mg. plus 150 mg.) of bismuth glycolylarsanilate and chloroquine daily for 15 days, with stool examinations at 7 and 15 days. Group 2 was given three bismuth glycolylarsanilate and chloroquine (400 mg. plus 100 mg.) tablets daily for three days followed by one day of rest. Then two tablets were given daily for eight days. Results are indicated in table 3.

As indicated by table 3, not only did group 1 show the most favorable results reported from any amebacide included in this study, but side-effects produced by the combination of bismuth glycolylarsanilate and chloroquine in the proportion of 500 mg. to 150 mg. administered twice daily were far fewer and less marked than with group 2. Complaints reported by both groups are summarized as follows:

	Group 1	Group 2
Nausea	7	20
Vomiting	1	16
Pruritus ani	4	7
Lower left quadrant pain	2	13
Diarrhea	19	14

Table 4 summarizes the patient response and laboratory findings after the first and second weeks of treatment. It indicates a very satisfactory subsidence of clinical symptoms, and the laboratory results reveal that this combination is effective even when some degree of liver involvement is evident.

Group 1 patients were carefully instructed to space the taking of the drug at 12 hour intervals. I believe that this point is of great importance in keeping side-effects at a minimum and that side-effects may be further reduced by the administration of vitamin B complex.

In view of the poor results obtained with the 400 mg. of bismuth glycolylarsanilate and 100 mg. of choroquine tablets administered three times daily, further work with this type of tablet was discontinued. The remaining 30 patients with stools still positive for cysts were treated with three tablets of 500 mg. of bismuth glycolylarsanilate three times daily for 15 days, after which they received two tablets of the combination daily for another 15 day period. At the end of the course, the stools in 13 cases became negative and in the remaining 17 treatment was continued in the following manner: one tablet of bismuth glycolylarsanilate and chloroquine was given twice daily for 15 days followed by one tablet of bismuth glycolylarsanilate three times daily for the next 15 days.

As a result of this third course of treatment stools in six more cases were negative for both cysts and trophozoites. The 11 patients with positive stools were then transferred to combined treatment with chloroquine and oxytetracycline, as explained previously, but the stools of only two were finally reported as negative. There is some doubt in my mind in regard to the remaining nine patients, all of whom were women of nervous temperament and who may not have followed instructions faithfully.

The results in all the 102 patients treated with bismuth glycolylarsanilate and chloroquine revealed that 91, or 89.2%, finally became free of cysts.

CONCLUSIONS

With few exceptions, all patients have been observed during a six month control period, and to date, there have been no relapses. The patients treated with bismuth glycolylarsanilate, chloroquine, and oxytetracycline will be kept under observation for a full 12 month period, but unless the final control examination reveals an unexpectedly large percentage of relapses, the following conclusions should hold true:

1. The combination of bismuth glycolylarsanilate and chloroquine (milibis®-aralen®) in the proportion of 500 mg. to 150 mg. is the most effective amebacide covered by this study. 2. The combination of 500 mg. of bismuth glycolylarsanilate and 150 mg. of chloroquine administered twice daily is preferable to 400 mg. of bismuth glycolylarsanilate and 100 mg. of chloroquine administered three times daily both from the point of view of efficacy and of minimal side-effects. 3. The combination of 500 mg. of bismuth glycolylarsanilate and 150 mg. of chloroquine when administered twice daily for 15 days is well tolerated, and the few side-effects occasionally observed do not necessitate the interruption of treatment. 4. The combination of the nonabsorbable arsenical, bismuth glycolylarsanilate, with the highly absorbable chloroquine is a logical and effective treatment for amebiasis, which should be considered as a systemic and not a purely intestinal disease.

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TABLE 4.—*Summary of Clinical and Laboratory Findings After the First and Second Weeks of Treatment with Chloroquine and Bismuth Glycolylarsanilate*

Clinical Complaints and Symptoms	Before Treatment		First Week		Second Week	
	No.	%	No.	%	No.	%
Diarrhea	98	96.1	0	...	0	...
Nausea	80	78.4	27	26.5	7	6.9
Chills	76	74.5	0	...	0	...
Colic and epigastric pains	100	98.0	40	39.2	30	29.4
Tender liver	81	79.4	12	11.8	12	11.8
Tender colon	102	100.0	12	11.8	11	10.8
Laboratory Findings						
Leukocytosis	74	72.5	4	3.9	4	3.9
Anemia	97	95.1	51*	...	60*	...
Cephalin flocculation 1+ in 48 hr.	90	88.2	48	47.1	37	36.3
Cephalin flocculation 2+ in 48 hr.	12	11.8	0	...	0	...
High icterus index	81	79.4	14	13.7	4	3.9
Cysts of E. histolytica	102	100.0	69	67.6	30	29.4

* These patients were showing improvement in blood findings.

Growing Responsibility.—The responsibility which we shoulder increases with every new [medical] discovery. When there was no efficient treatment for meningitis it did not matter whether we made the diagnosis on the first day or the fifth. Today it may literally be of vital importance. The same responsibility concerns us in all that we do, with chronic illness as well as with acute. Advances in surgery are not solely the concern of the surgeon, but place a new responsibility on the practitioner to recognize the early stages of disease which may be amenable to the surgeon's newer skills.—Robert Platt, M.D., Wisdom Is Not Enough: Reflections on the Art and Science of Medicine, *The Lancet*, Nov. 15, 1952.

THE CASE AGAINST HEPATIC ARTERY LIGATION IN PORTAL HYPERTENSION

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and
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Considerable interest has recently been given to the suggestion of ligating the hepatic artery for the treatment of portal hypertension.[1] On first thought there would seem to be no justification for such a procedure. There is, however, enough experimental background for this operation to make it seem logical and attractive. We too have succumbed to its temptations and have done a few ligations. These have been sufficient to indicate certain shortcomings that were not at first anticipated. The net results were not wholly bad but were such that it is thought the operation should be discontinued for the present. This communication is made to warn physicians that there may be some types of portal hypertension in which this procedure is indicated, but at present these indications are far from clear. In fact, to know which cases might be benefited seems impossible.

A fair evaluation of the operation must include the scientific background that indicates the benefits that might be obtained by hepatic artery ligation. This had its origin with the liver perfusion studies of Dr. F. C. Herrick, working in London Hospital nearly 50 years ago. These studies indicated that there was a relationship between hepatic arterial pressure and portal vein pressure. Herrick inferred that if the pressure in the hepatic artery of a portal hypertensive patient could be decreased, then the portal pressure would likewise be decreased. This decrease was shown to be much greater in the perfused cirrhotic liver than in the normal liver. It logically followed that this lowering of hepatic arterial pressure could be used to decrease the portal pressure.

This important observation on the perfusion pressures in normal and cirrhotic livers lay dormant for many years. So far as can be determined, there was no challenge or significant comment on it until 1928 when McIndoe's important monograph appeared. While McIndoe's work was primarily concerned with the vascular anatomy as shown by corrosion studies of the liver vascular bed, a few pressure perfusion studies were also included. It was noted that these did not confirm the relationships previously found by Herrick. It should be emphasized, however, that the feature that was not confirmed was the mathematical ratio cited by Herrick. The perfusion studies of McIndoe did indicate a definite relation between the arterial and portal pressures. In the livers of cirrhotic patients there was a corresponding increase in portal venous pressure with a rise in hepatic arterial flow. The ratio varied somewhat, but nevertheless the fundamental relation was always present.

The effect of increased hepatic arterial flow was again explored by Dock in 1942. This investigator criticized former perfusion studies because many were not performed under physiological conditions. Dock used kerosene in the perfusions to avoid any errors that might occur because of edema resulting from the perfusion fluids. The pressures used in both the hepatic artery and the portal vein were kept in a range that was present during life. This work again confirmed the definite relationship between portal flow and hepatic arterial pressure in cirrhotic livers.

Recently we were engaged with Egbert and Raber in further liver perfusion studies on cirrhotic and normal livers. Some 11 cirrhotic and 4 normal livers were thus studied using varied pressures and amounts of fluid passing through the liver. Some of the results have already been reported.[1c] Others are noted and discussed in this communication.

HEPATIC ARTERY OCCLUSION

As indicated there is a definite relationship in the perfused cirrhotic liver between the hepatic arterial pressure and portal vein pressure (and flow). When the arterial pressure is increased, the same occurs in the portal vein. With a decrease in arterial flow and pressure the portal pressure drops and more portal blood flows through the liver. No such significant relationship was found in normal livers.

This is graphically indicated in figure 1. Here it will be noted that in the normal liver there is no significant change in portal flow as the hepatic arterial pressure increases from zero to 150 mm. Hg. The curve shown indicates average figures on three normal livers. During these tests the portal vein pressures were kept at a constant perfusion pressure of 200 mm. H_2O. The same is true for the cirrhotic livers represented in the lower solid line (three livers). The curve representing the cirrhotic livers is much the same as that for the normal except that it starts much farther down the scale of portal vein flow. It quickly reaches the zero flow line, which it tends to parallel. In fact, several of the perfused cirrhotic livers gave a backflow into the portal vein (dotted line). This reversal of flow into the portal vein from the hepatic artery perfusion was characteristic for high arterial pressures (180 to 200 mm. Hg). No such tendency to backflow was noted in normal livers, possibly because the pressure was too far above the base line.

This analysis so far suggests that ligation or at least partial occlusion might be indicated in cases of portal

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1. (*a*) Rienhoff, W. F., Jr.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension with a Report of 6 Cases: Preliminary Report, Bull. Johns Hopkins Hosp. **88**: 368, 1951. (*b*) Berman, J. K.; Koenig, H., and Muller, L. P.: Ligation of Hepatic and Splenic Arteries in the Treatment of Portal Hypertension: Ligation in Atrophic Cirrhosis of the Liver, A. M. A. Arch. Surg. **63**: 379 (Sept.) 1951. (*c*) Egbert, H. L., and Raber, R. M.: The Physiologic Effect of Hepatic Artery and Portal Vein Ligation: Results of Perfusion Studies and Observations on Patients at Operation, in Surgical Forum, Clinical Congress of the American College of Surgeons, 1951, Philadelphia, W. B. Saunders Company, 1952, p. 153.

hypertension. However, as this thesis is probed further some disconcerting findings appear. First of these is the fact that, though occlusion of the perfused hepatic artery decreases the portal pressure and allows a greater portal flow, no such change was noted in the live patient. Under carefully controlled conditions we have occluded the hepatic artery of patients with portal hypertensions between 450 and 600 mm. H_2O. No significant change in portal pressure was noted. Sometimes the pressure would show a resultant rise of a few millimeters, and at other times it might fall a like amount. This failure to demonstrate a constant drop in portal pressure as a result of temporary occlusion of the hepatic artery has been noted by others.[2]

In passing it might be worth reporting the result of hepatic artery occlusion in normal patients. On four occasions we have temporarily occluded this artery in patients undergoing operation for cholecystectomy or gastric resection. A manometric reading during the arterial interruption indicated no constant change in portal pressure. The following conclusion then seems warranted. In

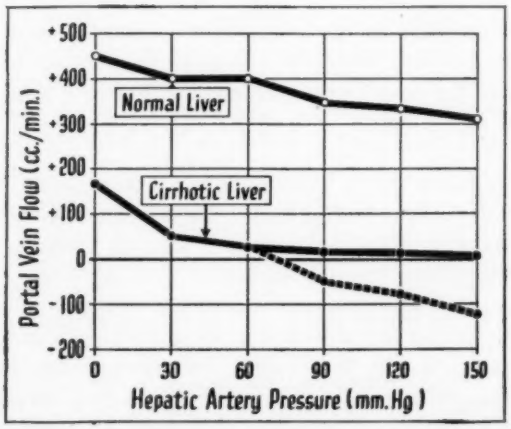

Fig. 1.—Effect of hepatic artery pressure on portal flow in perfused liver (portal vein pressure constant at 200 mm. H_2O). It is noted that in the cirrhotic liver the portal flow quickly approaches zero under normal hepatic arterial pressures. Several perfused cirrhotic livers actually gave a backflow into the portal vein as indicated by the dotted line. This sluggish flow may well be the cause of the frequently associated portal thrombosis.

the operative patient it has not been shown that occlusion or partial occlusion of the hepatic artery decreases the portal pressure.

The next feature of interest is the physiological state of the liver itself. Practically all patients with intrahepatic portal hypertension have profound liver damage. It is then of utmost importance to learn how hepatic artery ligation may affect this hepatic insufficiency. Any physiological improvement brought about by ligation must be directly related to an increased flow of blood through the liver. Such information, of course, is not available in the living patient, but an analysis of the perfusion studies is quite interesting. Does the occlusion of the hepatic artery allow more total blood to pass through the liver even though it may all be from the portal vein? An analysis of this point is shown in figure 2. Here against a constant portal vein perfusion pressure of 200 mm. H_2O is plotted the actual flow through the liver under varying hepatic arterial pressures. The normal curve represents average values on two livers, while three cirrhotic livers underwent the same perfusion variations and make up the lower curve. Here it will be noted that in all, but particularly in the cirrhotic, livers there is an ever-increasing flow of fluid through the liver with each increase in arterial pressure. Likewise a profound decrease in liver blood flow is noted as the arterial pressure is diminished. It would therefore seem that diminishing the arterial flow

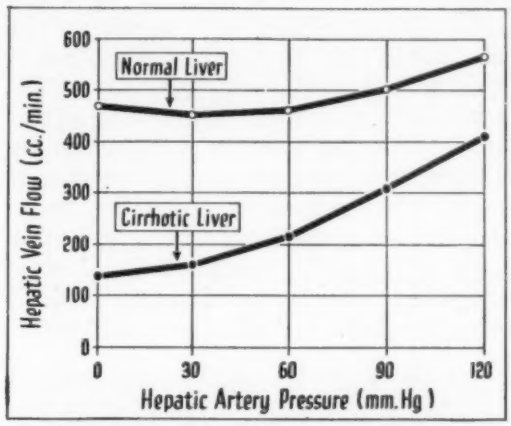

Fig. 2.—Effect of hepatic arterial pressure on total blood flow through perfused liver. With the portal pressure at 200 mm. H_2O it is seen that the flow through the liver is dependent on and proportional to the hepatic arterial pressure in both normal and cirrhotic livers. A variation of the 200 mm. H_2O portal vein back pressure did not alter these curves.

to a badly crippled liver is an ill-advised procedure. The liver is in need of every bit of blood it can receive. A further analysis of this same query into the blood supply of the cirrhotic liver is shown in figure 3. Here the hepatic arterial perfusion pressure was held at a constant 120 mm. Hg, and the portal vein perfusion pressures were varied from 150 to 350 mm. H_2O. Again the average values from two normal livers and three cirrhotic livers were used. A very significant finding is noted. The flow through the normal livers rose rapidly and was directly

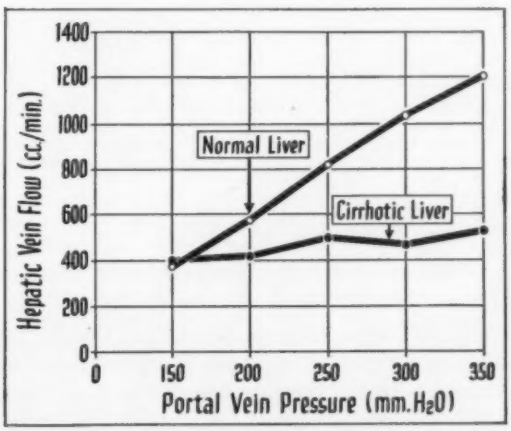

Fig. 3.—Effect of increasing portal vein pressure on total blood flow through perfused liver. With hepatic arterial pressure held constant at 120 mm. Hg it is noted that the flow through the normal liver is directly proportional to the portal vein pressure while the cirrhotic liver flow changes but little with an ever-increasing portal vein pressure.

proportional to the pressure in the portal vein. This same relationship was not found in the three cirrhotic livers, where a doubling of the portal pressure caused only a

2. Child, C. G., III, and Egbert, H. L.: Personal communication to the author.

slight increase in flow through the liver. The number of perfusions indicating this feature are too few to allow complete acceptance. Nevertheless the inference is inescapable that an ever-increasing portal pressure forces more portal blood through a normal liver but is unable to significantly change the low rate of flow through the cirrhotic liver. As indicated we as well as others, have found that a decrease in perfusion hepatic arterial pressure allows an increased portal flow. This omits discussion of the actual blood flow through the liver. What has not been said before is that when the arterial perfusion pressure is diminished so is the flow through the liver (fig. 2). Therefore, when there is any danger of hepatic insufficiency it would seem foolhardy to deprive the liver of its only remaining effective blood supply. To this argument must be added the already mentioned fact that in cirrhotic patients there is no evidence that occluding the hepatic artery effectively diminishes portal hypertension.

Fig. 4.—Portal vein of an advanced cirrhotic portal hypertensive patient. The vein is practically occluded by a thrombus, which is of old and recent origin.

THROMBOSIS OF PORTAL VEIN

It has been a source of considerable bewilderment to find portal veins already thrombosed when exposed for operative portacaval anastomosis. Of the last four portal veins that were explored in preparation for an end-to-side anastomosis with the inferior vena cava there were two that were half occluded with a thrombus (fig. 4). Two similar cases were noted recently by Dr. Harris B. Shumacker at the University Hospitals. These were completely thrombosed and apparently were undergoing early canalization. This experience is admittedly small, but it indicates that a part, perhaps a large part, of portal veins will be found thrombosed at operation. Surely no one would advocate the ligation of the hepatic artery in such a situation. It would be inviting certain disaster.

Thrombosis of the portal vein in patients with portal hypertension has been frequently noted and discussed by others.[3] It has invariably been suggested that this thrombosis was the cause of the portal hypertension. There may be such cases, but we have not had an opportunity to study them. Quite the reverse seemed to be the actual condition, with the thrombus an innocent addition. The thrombus probably was present because of an extremely sluggish portal circulation (fig. 1). The portal vein has been repeatedly occluded at operation on cirrhotic hypertensive patients and no significant change in portal pressure has been noted. This was proof, at least in these cases, that blood flow in the portal vein was at a low ebb or complete standstill and was inviting thrombosis. In one instance the portal vein was actually ligated on the premise that the blood in this particular vessel was flowing backward.

This same line of reasoning has confirmation in the work of Child [4] and others.[5] These definitely indicate that the portal veins of men and animals under certain conditions may be safely occluded. Following this occlusion portal hypertension immediately appears, which subsides again to a completely normal pressure in one or two weeks. It therefore is quite difficult to rationalize the so-called extrahepatic portal hypertension as having its origin in a portal thrombosis or occlusion. It seems far more logical to assume that such thrombosis results from an extremely sluggish flow in the hypertensive portal vein.

OBJECTIONS TO LIGATION

One of the principal objections to the various operations that have been proposed for portal hypertension is that they are all long, time-consuming endeavors, which are hard on both patient and surgeon. This becomes even more important when it is realized that many of these patients are in desperate condition as a result of repeated hemorrhages and a badly damaged liver. Therefore, any simplification of treatment is eagerly sought by all. It was the hope of those undertaking hepatic artery ligation that this would solve this particular phase of the problem. It would substitute a simple 30 minute operation for a protracted portacaval shunt or resection in these extremely ill patients. These hopes and expectations were short-lived. Admittedly, in a normal person the ligation of the hepatic and possibly left gastric arteries are simple enough. However, in cirrhotic patients with gnarled varicosities filling the thickened edematous and distorted gastrohepatic omentum, the operation may be extremely trying and difficult. It may require all possible technical skill and ability. It may require two or three hours for its successful execution. It is a formidable procedure not to be entered on lightly.

3. Whipple, A. O.: The Problem of Portal Hypertension in Relation to the Hepatosplenopathies: E. Starr Judd Lecture, Ann. Surg. **122**: 449, 1945. Rousselot, L. M.: The Late Phase of Congestive Splenomegaly (Banti's Syndrome) with Hematemesis but Without Cirrhosis of the Liver: Further Observations on Etiology of Banti's Syndrome and Effect on Prognosis of Certain Variations in Portal Venous Pattern, Surgery **8**: 34, 1940. Blakemore, A. H., and Fitzpatrick, H. F.: The Surgical Management of the Post-Splenectomy Bleeder with Extra-Hepatic Portal Hypertension, Ann. Surg. **134**: 420, 1951.

4. Child, C. G., III, and others: Pancreaticoduodenectomy with Resection of the Portal Vein in the Macaca Mulatta Monkey and in Man, Surg., Gynec. & Obst. **94**: 31, 1952.

5. Douglass, T. C., and others: Attempts at the Experimental Production of Portal Hypertension, A. M. A. Arch. Surg. **62**: 785 (June) 1951. Peck, M. E., and Grover, R. F.: Cardiovascular Responses to Acute Ligation of Portal Vein, ibid. **64**: 665 (May) 1952.

The desirability of preserving all possible arterial blood flow to the damaged liver has been mentioned earlier in this discussion. As indicated by the perfusion studies the only hope of improving blood supply to the cirrhotic liver would seem to be by supplying more, not less, arterial blood (fig. 2 and 3). It must, therefore, require a strong and healthy liver to survive the assault of operative interference with its arterial blood supply. Medical literature is replete with reports of deaths following accidental hepatic artery ligation during biliary tract surgery. Admittedly these occurred when the terminal artery was ligated rather than occluded near its origin. It is strange that this hazard has not been stressed by those advocating arterial ligation for it certainly is not a rare complication. We are aware of three such deaths, including the one completely described by one of us (D. R.) and Egbert.[6] These all had a similar pattern with hyperpyrexia and death a few days following operation. The operation in each case consisted of ligation of the hepatic artery near its origin, along with splenic or left gastric occlusion. The pathological picture was uniform with extensive infarction of the cirrhotic liver nodules.

It is, of course, impossible to name all the factors that allow one liver to remain unscathed following hepatic artery ligation while another receives a lethal infarction. Undoubtedly aberrant and collateral blood supply are the deciding factors. It cannot be determined at the operative examination what the extent of this collateral blood supply may be. Therefore, the operator cannot know the sufficiency of a given blood supply. Without this information he cannot know which patients can be safely ligated and which might die following this procedure. Michels [7] has recently reemphasized the great variability of blood supply to the liver, thus precluding any possibility of scientific or accurate appraisal of the situation. Other unknowns must, of course, concern hepatic reserve and the extent of liver damage. Until a better understanding can be obtained of the physiological problems at hand it would seem too hazardous to advocate the treatment of portal hypertension by hepatic artery ligation. The literature attests that some patients may survive and possibly show clinical improvement following ligation. Whether this improvement is spontaneous or the result of a lessened arterial flow to the liver is certainly debatable. Nevertheless some patients also die because of this procedure, and if the present trend continues unchecked the literature will also attest to many deaths.

SUMMARY

Perfusion studies on cirrhotic human livers indicate that the pressure in the portal vein is decreased with a decrease or obliteration of the hepatic arterial pressure. This is the basis for the rationale of hepatic artery ligation in the treatment of portal hypertension. Omitted from consideration has been the fact that with this decreased portal and hepatic arterial pressure there results a great decrease in the blood flow through the liver. The damaged liver seen in most of these cases of portal hypertension requires the greatest possible blood supply. Therefore any procedure that decreases this flow would seem to be very detrimental. There is no way to accurately estimate the physiological state of the liver at the time of operation in order to determine which patient may survive an hepatic artery ligation and which will die as a result of the operation.

From perfusion studies it has been shown that blood flow through the cirrhotic liver is proportional to the hepatic arterial supply and is affected very little by the portal pressure. In the portal hypertensive patient it has been impossible to produce a consistent decrease in portal pressure by temporary obliteration of the hepatic artery. Many portal veins in this condition are thrombosed. Surely there could be no thought of removing the only other source of the blood flow to the liver. It would be well to mention that partial or complete portal thrombosis might easily be overlooked when doing an hepatic artery ligation.

One of the features that has attracted many physicians to the operation has been the thought that it substituted a simple short procedure for a hazardous long one. This may be true in the occasional case, but in the usual one it is long, arduous, and technically very difficult. The dangers of possible liver infarction have not been emphasized. A few deaths have already resulted from this operation, and many more will occur unless each case is considered carefully from a physiological point of view. The operation should be abandoned until it can be determined which patients it might possibly help and in which it is definitely contraindicated.

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6. Rosenbaum, D., and Egbert, H. L.: Liver Necrosis and Death Following Hepatic Artery Ligation, J. A. M. A. **149**: 1210 (July 26) 1952.
7. Michels, N. A.: The Hepatic, Cystic and Retroduodenal Arteries and Their Relations to the Biliary Ducts, with Samples of Entire Celiacal Blood Supply, Ann. Surg. **133**: 503, 1951.

Rectal Complaints.—One need only note the great variety of pile ointments, suppositories and other types of rectal medication on the shelves of drug stores to realize the frequency of rectal complaints. In addition to the prevalence of proctologic disorders, there is another reason why the sale of such proprietary products has reached tremendous proportions. Are we not, as physicians, responsible for driving our patients to seek help from the sales clerk and from charlatans—because of our indifference, our failure to examine properly, diagnose correctly or to prescribe intelligently? Too often the patient's rectal complaints are met with a shrug of the shoulders, a mumbled guess that it is probably due to piles. He is then handed a sample of one of the numerous preparations with which the doctor's office is deluged, advised to take some mineral oil and gently ushered out of the office with the following admonition "Use these and if it isn't any better in a couple of days, let me know." Yet last year thousands of individuals died from cancer of the rectum and colon.

Shallenberger and Fisher in an exhibit presented at the American Medical Association Convention in Chicago, June, 1952, stated that 65% of 4,500 consecutive sigmoidoscopic examinations of unselected patients shows some abnormal condition. Two and one-half per cent of patients examined were found to have a malignant tumor in that portion of the bowel viewed through a proctoscope. Since the incidence of anal, rectal and lower sigmoidal disease is so high, does it not behoove us to make a conscious endeavor to examine our patients thoroughly, especially those with rectal complaints? It is a sad commentary that almost one-half of patients with carcinoma of the rectum have been treated for some rectal condition other than cancer before the true nature of the disease was determined. It may be stated categorically that any rectal symptom, any deviation from the normal, demands a complete and thorough investigation.—Durand Smith, M.D., Office Proctology, *The Medical Clinics of North America*, January, 1953.

INDICATIONS FOR LIVER BIOPSY

Victor M. Sborov, M.D.
and
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In the past 10 years a number of important advances have been made in our understanding of diseases affecting the liver. Although these advances have not resulted in dramatic cures, we are now in a much more substantial position in our comprehension of the pathology, the diagnosis, and the prognosis of liver disease. With an appreciation of the widespread occurrence of liver disease, particularly of an infectious character, and a beginning knowledge of the important role played by the liver in nutrition, detoxification and digestion, a very great increase of experimental work has been undertaken to widen the scope of information of this important organ. One of the fundamental contributions to our progress has been the increased use of the liver biopsy as a diagnostic and investigative tool.

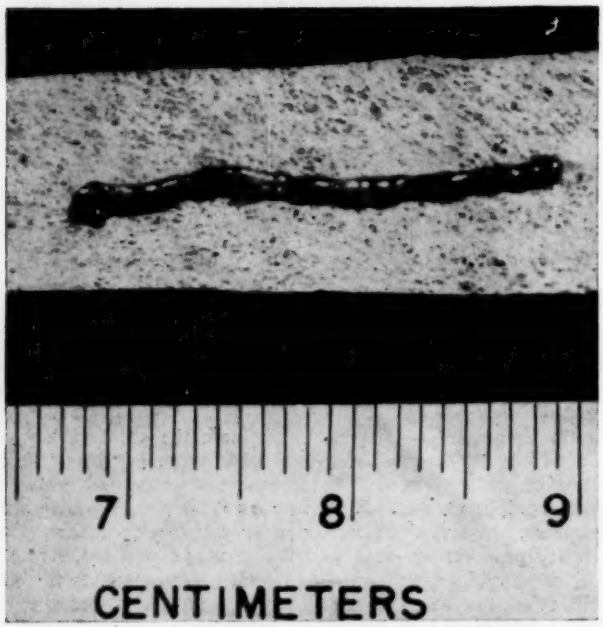

Fig. 1.—Liver specimen obtained with Vim-Silverman needle.

Although the first liver biopsy was done in 1895, it was not until the middle 1940's that this procedure began to be used widely.[1] Several instruments have been developed for the purpose of obtaining a specimen of the liver for histological study.[2] Most of the instruments now in use involve the principle of penetration of the liver with a needle or a trocar, following which a small piece of tissue is obtained for microscopic study either with a rotatory cutting motion or by aspiration. Local anesthesia is used with either the subcostal or the intercostal approach to the liver.[1a] The advocates of the subcostal approach maintain that it is a safer technique because it does not involve fixation of the needle between the ribs. With this method the needle can migrate freely with respiration during the entire procedure.[3] The principal disadvantage, however, is that the subcostal approach cannot be used with confidence when the liver is not palpable.

The transpleural or intercostal approach, on the other hand, permits a biopsy of the liver even when it cannot be demonstrated below the costal margin. With the latter modification, however, it is mandatory that respirations be stopped at the time the needle is inserted through the intercostal space, since fixation of the needle by the ribs may result in tearing of the liver capsule. Speed is therefore of greatest importance, and changes of the needle and the technique have been made to meet this requirement.[4]

In a discussion of techniques, it is difficult to compare one practice with another. Much depends upon the experience and skill of the individual operator. Such techniques are usually developed by repeated modifications as experience is gained; the resultant method is usually the one that will give the most satisfactory number of specimens with the fewest complications.

The specimen obtained with the Vim-Silverman needle varies from 1 to 3 cm. in length and from 1 to 2 mm. in width. (fig. 1). In such a biopsy specimen 8 to 15 lobules of liver can be visualized and upwards of 50 serial sections, 5 μ thick, can be obtained. With this, a fair estimate can be made of a diffuse process involving the entire liver.

The use of a needle for biopsy rather than a surgical wedge has been advocated even when a laparotomy is done. At laparotomy, however, because of the manipulation of the liver prior to the time of biopsy, artifacts may result due to pressure and anoxic changes. This could be avoided by use of a needle soon after the liver is exposed.[5]

It has been shown that when needle biopsy specimens and serial sections at postmortem are compared, there is a high degree of reliability in procuring a representative piece of liver tissue with the needle.[6] This has been especially so when there is a diffuse process involving the entire liver. Such diffuse processes include toxic

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Owing to lack of space, some of the bibliographic references have been omitted from THE JOURNAL and will be included in the authors' reprints.

From the Department of Hepatic and Metabolic Diseases, Army Medical Service Graduate School and the Laboratory Service, Walter Reed Army Hospital.

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hepatitis, viral hepatitis, fatty liver, and portal cirrhosis. It is entirely possible, on the other hand, that a tumor nodule or abscess may be missed completely even on repeated sampling of the liver.

COMPLICATIONS OF LIVER BIOPSY

Hemorrhage.—The complication most to be feared from a liver biopsy is hemorrhage. Such a hemorrhage may, and does on occasion, cause death to the patient.[7] The bleeding usually results from a tear in the liver capsule. A hemorrhage may also result if a blood vessel is lacerated within the substance of the liver. Warning of a catastrophe of this kind is usually not obvious for the first few hours because external bleeding is usually minimal. Arterial or venous bleeding following a liver biopsy may be slow, and the manifestations of shock may appear several hours following the biopsy. It becomes of paramount importance, therefore, that the patient be observed carefully for a minimum of 24 hours following biopsy. This observation should include frequent measurement of blood pressure, pulse, and respiration. It has been shown in humans that there may be slow blood loss over a period of hours without any increase in pulse rate or drop in blood pressure. Then, rather suddenly, either with a shift of position or with further bleeding, profound shock will develop.[8] We have observed an example of this in the present series. Following liver biopsy in a young patient with hepatitis, blood pressure and pulse were maintained at normal levels until 24 hours after completion of the procedure. Suddenly, a few moments after the last blood pressure measurement, the patient became tremulous and pallid and was noted to be in shock. This was fortunately detected early, and with vigorous measures a fatality was probably avoided. It must be emphasized that, because of the necessary precautions, liver biopsy can be performed only in hospitalized patients and should not be undertaken as an outpatient procedure.

Although it is not always possible to avoid accidental tearing of a blood vessel or the liver capsule, the complication of hemorrhage will be held to a minimum if a possible bleeding tendency in a patient who is to undergo biopsy can be evaluated accurately and the procedure is avoided when evidences of a hemorrhagic tendency are present. It is important in this connection to measure the bleeding, clotting, and prothrombin times on the day preceding the biopsy of the liver. A prolonged bleeding or clotting time or a prothrombin time of less than 50% of normal should warn against the use of the liver biopsy. An abnormally low platelet count should likewise serve as a contraindication. As a final measure of caution, it is recommended that each patient have one unit of blood crossmatched for emergency purposes prior to the time of the biopsy. In a series of 560 biopsies it has been necessary to make use of this blood on but two occasions.

Bile Peritonitis.—Another complication of the liver biopsy has been the development of bile peritonitis because of leakage of bile from a tear in the gallbladder or large bile ducts.[9] This latter complication is believed to be more likely to occur when there is obstruction of the common bile duct with deep jaundice. Under these circumstances the pressure in the biliary channels is probably high, and a tear of a biliary radical by the biopsy needle may result in bile leakage into the peritoneum. For this reason it has been recommended by some that biopsy of the liver be avoided in the presence of high-grade biliary obstruction.

Pulmonary Infection and Pneumothorax.—With the use of the intercostal approach and the passage of the biopsy instrument through the pleura and the diaphragm into the liver, it is possible that spread of infection might result. In one patient in the present series pneumonitis of the middle lobe of the right lung developed following biopsy of the liver. The patient had an upper respiratory infection at the time of biopsy, and 24 hours later fever, cough and absent breath sounds over the middle lobe of the right lung developed. It could not be established definitely, however, that this resulted from the biopsy. In this patient all of the physical and x-ray changes cleared within one week. Biopsy of the liver is

Fig. 2.—Liver specimen from a patient with obstructive jaundice. Circle shows inspissated bile filling a canaliculus. Note absence of liver cell necrosis. There is no cellular infiltrate (hemotoxylin and eosin, × 260).

contraindicated where there is known infection in the pathway of the needle.

Pneumothorax has also been reported as a complication of needle biopsy of the liver.[1e] Although critical efforts to find pneumothorax in our series have not been made, none have been called to the attention of the staff.

Pain.—In our experience pain at various sites at time of biopsy and following the biopsy has been the most frequent complication. It has occurred in 28% of cases (this figure is similar to the 30% reported elsewhere [1e]). The pain resulting from liver biopsy has not been a serious problem, but because of its frequency it

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has been the most prominent reason for disfavor of the procedure on the part of the patient. The pain of liver biopsy usually occurs in one of three sites. At the time of insertion of the needle into the liver, pain usually results that mimics that from a blow in the right upper quadrant or epigastrium. This pain is only momentary and disappears within a very few minutes. It may, however, persist for two or three hours and require analgesia.

The second site of pain is in the area entered by the biopsy needle. This discomfort may be present immediately after the biopsy or develop insidiously 1 to 2 hours later and persist for 8 to 12 hours. The pain is usually pleuritic and closely associated with respirations. On occasion it may cause marked distress. A patient may become panicky because breathing is painful and

Fig. 3.—Liver specimen from a patient with chronic viral hepatitis. There is an increase of fibrous tissue and mononuclear infiltrate in the portal space, with extension of the portal space into the liver lobule. There are foci of necrosis in hepatic parenchyma and minimal fatty metamorphosis (hematoxylin and eosin, × 80).

breath-holding is impossible. In this type of pain tetraethylammonium chloride has proved to be particularly helpful.[10] When it is given intravenously in a dose of 200 mg., immediate alleviation of pleuritic pain results in most instances. Once the pain is relieved, the patient can, with proper instruction, break up the unfortunate cycle of pain causing breath-holding followed by more pain when breath-holding is no longer possible. Although the effect of tetraethylammonium chloride is only transitory, it serves to reassure the patient that relief can be obtained rapidly if necessary.

A third locus of pain is that which appears in the right supraclavicular region. This causes no particular distress to the patient. It is most likely to be referred from the diaphragm and caused by an irritation of that structure by the biopsy needle. In most cases this is mild in character and has not by itself required analgesia.

The problem of pain following liver biopsy is not a major one. Although the routine use of preoperative analgesia has been advocated,[11] it is our belief that this can be dispensed with in most cases. If careful infiltration of the skin, pleura and the liver surface with 1% procaine is practiced, serious discomfort will be avoided in most instances. If a patient appears to be apprehensive prior to the biopsy, a sedative may be administered. When needed because of the resulting pain, tetraethylammonium chloride, meperidine (demerol®), or codeine and acetylsalicylic acid (aspirin) may be used. Because the liver biopsy is usually done when liver disease is suspected, morphine and barbiturates should be avoided as a routine precaution. The following summary shows the complications and the number of cases in which they were encountered by our department in 560 needle biopsies of the liver.

Deaths	0
Hemothorax	0
Hemoperitoneum	2
Bile peritonitis	2
Pneumothorax	0
Atelectasis, middle lobe of right lung	1
Pain in right chest or shoulder requiring analgesia	157

An analysis of the contraindications and complications of liver biopsy shows that, although there are small groups of patients in whom a biopsy cannot be performed regardless of the need, it can be used in most situations. The procedure is simple and readily available in most communities. Because of the ease of obtaining a biopsy, its use may be abused. It is therefore of some importance to ask, "Why do a liver biopsy?" Even with the best of precautions and the greatest of care, biopsy of the liver is not and never will be a completely innocuous procedure. Therefore present aspects of liver biopsy must be evaluated and the time and conditions needed for best results defined critically.

INDICATIONS FOR BIOPSY OF THE LIVER

To Diagnose Hepatomegaly of Unknown Etiology.—Use of liver biopsy in hepatomegaly of unknown etiology was demonstrated in a white veteran 29 years of age. He gave a history of schistosomiasis in 1942 and in the next seven years had recurrent episodes of hematuria, abdominal pain, and backache. The exact cause of the hematuria and backache had not been determined. In addition, the patient complained of increased fatigue over a period of three weeks. It was because of these symptoms that the patient was hospitalized. There had been no history of jaundice in the past. The patient was studied on the urology service, where a physical examination revealed a moderately obese person in no distress. He showed right costovertebral angle tenderness, and his liver was enlarged 6 cm. below the right costal margin and was moderately tender. The spleen was not palpated, and no ascites was present. The liver function tests were completely within normal limits except for a borderline result of a sulfobromophthalein (bromsulphalein®) test, with 6% retention in 45 minutes. The outstanding objective evidence of disease in this patient, therefore, was an enlarged, tender liver.

Because of the possibility of persistent schistosomiasis, a biopsy of the liver was performed. Histological section showed marked diffuse fatty metamorphosis of the liver. No exact etiology could be adduced from the biopsy, and the patient was treated with lipotropic agents.

To Differentiate Medical from Surgical Jaundice.—The problem of the differential diagnosis of jaundice is one that confronts both the internist and the surgeon on many occasions. An error in diagnosis resulting in surgery in the presence of parenchymatous liver disease may lead to death of the patient or to prolongation of his illness. An example of this was seen in a white man, 37 years of age, who complained of epigastric pain, anorexia, dark urine, jaundice, and fatigue for one week prior to his admission. There had been no nausea, vomiting, or diarrhea. Physical examination revealed deep icterus; the liver was found to be enlarged 2 fingerbreadths below the costal margin and moderately tender. The spleen was not palpated. Palmar erythema was noted along with numerous spider angiomas over the neck and shoulders. The laboratory tests showed a serum bilirubin elevated to 11.3 mg. per 100 cc. The sulfobromophthalein retention was 66% in 45 minutes, but the results of thymol turbidity and cephalin cholesterol flocculation tests were normal. The prebiopsy diagnosis was viral hepatitis. The liver biopsy revealed biliary pigment in the liver cells around the central vein, inspissated bile in the small canaliculi, and absence of significant necrosis or cellular infiltrate in the liver lobules (fig. 2). An operation soon thereafter revealed carcinoma of the head of the pancreas.

To Establish the Diagnosis of Chronic Viral Hepatitis.—Although the histological picture of chronic viral hepatitis is not yet clearly established, it is believed that a biopsy of the liver is mandatory to ascertain whether hepatic abnormality is present in the patient who manifests residual symptoms after an episode of acute viral hepatitis. Such a patient may or may not show objective biochemical evidences of disease. A 29-year-old white man was studied who had acute viral hepatitis two years prior to the present admission. He showed a gradual improvement of his acute hepatitis over a three month period. After that time, however, he complained of recurrent symptoms of fatigue, irritability, and increased frequency of bowel movements. He had intermittent scleral jaundice but no weight loss or anorexia. The physical examination revealed a nontender liver, which was palpable 6 cm. below the costal margin. The spleen was slightly enlarged. There was no edema, ascites, or spider nevi. The total serum bilirubin was slightly elevated to 1.36 mg. per 100 cc. The sulfobromophthalein test showed 24.9% retention in 45 minutes, the thymol turbidity was elevated to 5.9 units, but the cephalin cholesterol flocculation was normal. A liver biopsy showed a pathological process confined to the portal space. There was increased mononuclear infiltration and proliferation of bile ducts, with extension of the portal space into the surrounding parenchyma (fig. 3). It was possible by means of repeated liver biopsies to follow this patient during various courses of therapy and to determine the effects of this therapy on the structure of the liver.

To Diagnose Congenital Anomalies Involving the Liver.—A 23-year-old white woman was seen who had been sickly and anemic throughout her entire childhood. At the age of 16 she had the onset of chills, fever, and abdominal pain. These recurred periodically until the time of her present hospitalization. A diagnosis of Banti's syndrome with hypersplenism had been made previously. On admission her chief complaint was right upper quadrant pain radiating to the right shoulder. Physical examination revealed the patient to be chronically ill. She was lethargic and pale. Her temperature was 101 F, and many small spider nevi were noted over her neck and shoulders. Her liver was enlarged 5 cm. below the right costal margin in the midclavicular line, with 2+ tenderness. Her spleen was enlarged 9 cm. below the costal margin. There was no ascites or peripheral edema present, and no palmar erythema was noted. The serum bilirubin level was slightly elevated, with the one-minute value 0.32 mg. per 100 cc. and the total value 1.08 mg. per 100 cc. There was 16% retention of sulfobromophthalein in 45 minutes; the thymol turbidity was 5.2 units; and the cephalin cholesterol flocculation was 2+ in 48 hours. The liver biopsy specimen from this patient showed encysted bilirubin trapped in blind pouches, and diffuse portal fibrosis was found throughout (fig. 4). A diagnosis of cystic disease of the liver was made. The patient died within the next two months of hepatic failure.

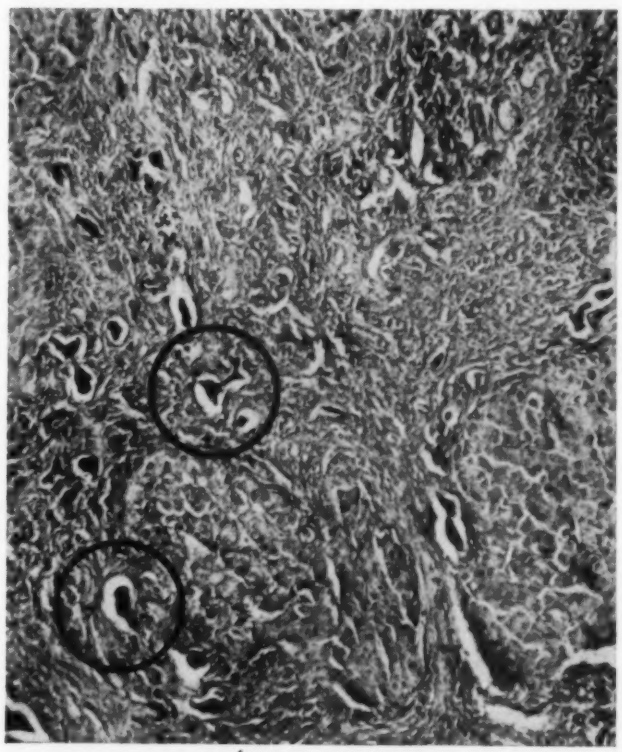

Fig. 4.—Liver specimen from a patient with cystic disease of the liver. There are blind pouches containing bilirubin (circles) and diffuse hepatic fibrosis (hemotoxylin and eosin, × 80).

To Establish the Hepatic Status in a Patient with Congestive Splenomegaly.—It is important to determine the histological status of the liver in a patient with congestive splenomegaly prior to the institution of sur-

gery. A 19-year-old white youth noted the onset of fatigability one month prior to the present admission. Three months prior to the present hospitalization he had been exposed to heavy carbon tetrachloride fumes. This was followed by nausea, vomiting, and right upper quadrant pain. Two tarry stools were noted by the patient in the week prior to admission. Physical examination revealed generalized pallor. No jaundice was noted. Spider nevi were seen on both arms. The spleen was enlarged 12 cm. below the costal margin. The liver was not enlarged or tender. Ascites and edema were not present. The serum bilirubin level was normal, but there was 18% sulfobromophthalein retention in 45 minutes. The thymol turbidity and cephalin cholesterol flocculation were within normal limits. The liver biopsy revealed marked irregular scarring with extensive bile duct proliferation. There were no evidences of necrosis

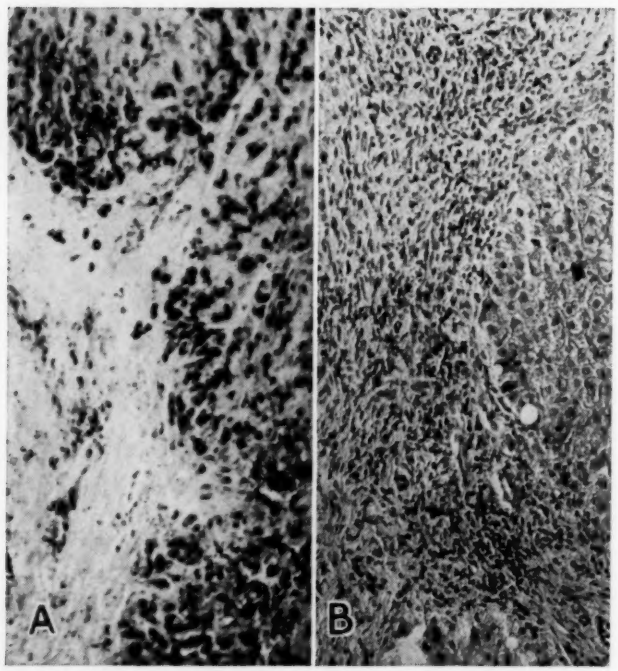

Fig. 5.—Liver specimen from a patient with hemochromatosis of the liver. Iron stain is seen before (*A*) and after (*B*) removal of iron from the liver through repeated phlebotomies. Note the persistence of fibrous tissue after iron removal (× 75).

or residual inflammatory activity in the liver. A portacaval shunt was performed in this patient without complication. The patient has remained well since.

To Establish the Prognosis of Prolonged Jaundice.—In our series the problem of prolonged jaundice was encountered in a 33-year-old white woman who noted the onset of colicky right upper quadrant pain five years prior to her present admission. She was not jaundiced initially but when the colic recurred repeatedly, cholecystectomy was performed four years prior to the current admission. At that time gallstones were found. A second operation was done six weeks after the first surgery because of the onset of jaundice. At the second operation a common duct stricture was repaired. There were recurrent chills, fever and jaundice, which persisted, and surgical exploration was done again 16 months later. An adhesive annular stricture of the ampulla of Vater was found and corrected. Nine months later, however, the patient was again operated on because of recurrent jaundice. Since the last procedure, chills and fever had recurred at weekly intervals, with persistent jaundice. These complaints resulted in her present admission. Physical examination revealed the patient to be poorly nourished, and slight jaundice was present. The liver was enlarged 15 cm. below the costal margin and was slightly tender. No edema or ascites was noted. The spleen was not enlarged. A one-minute serum bilirubin level was 1.78 mg. per 100 cc., with a total of 2.88 mg. per 100 cc. The sulfabromophthalein retention was 36% in 45 minutes, and the thymol turbidity was elevated to 6.1 units. A biopsy of the liver in this patient revealed marked portal scarring with ductal proliferation. There was abnormal architecture with normal liver cells.

To Establish the Diagnosis of Hemochromatosis.—A white man, aged 47, was studied because of fatigue, jaundice, anorexia, weight loss, and unexplained hepatomegaly of nine months' duration. A malignant growth in the urinary bladder had been resected three years prior to the present illness. There was a history of moderate alcohol consumption for several years. Physical examination revealed no jaundice. The liver was 7 cm. below the costal margin and was moderately tender. Palmer erythema was noted with a few spider nevi over the shoulders. There was no gynecomastia or skin pigmentation. The spleen was enlarged 3 cm. below the costal margin. Results of liver function tests were within normal limits except for 14% sulfobromophthalein retention and thymol turbidity slightly elevated to 4.4 units. The patient had a diabetic glucose tolerance curve, although sugar was not detected in his urine. A serum iron level elevated to 280 μg per 100 cc. was also found. The liver sections revealed marked infiltration of the liver cells with iron pigment and diffuse portal fibrosis (fig. 5*A*). This patient was bled of approximately 30,000 cc. of blood in a 14 month period. In this period the liver function tests returned to normal, but the liver size remained unchanged. A repeat liver biopsy showed virtually complete absence of iron in the liver (fig. 5*B*). Removal of iron from the liver by repeated phlebotomies has been previously demonstrated by Davis and Arrowsmith.[12]

COMMENT

Liver biopsy has now been demonstrated to be a useful tool in the diagnosis and the prognosis of liver disease.[13] It has also proved to be valuable in clinical investigation.[14] This procedure should be used freely where indicated and should result in material benefit to the patient under a wide variety of circumstances. As with other investigative methods, however, it not only creates new opportunities but stimulates new questions. It also serves to reemphasize questions that have been raised in the past and heretofore not adequately solved.

One of the very important questions that has been raised in connection with biopsy of the liver has been, "What constitutes a normal liver?" Classic textbook examples show the end stages of liver disease and of other well-defined conditions involving the liver. Descriptions of normal liver cells and normal hepatic architecture are also available. There, however, the information on

the liver stops. If it is remembered that most of the classic information comes from postmortem material, it can be better appreciated that this material relates, for the most part, to a condition resulting in death to the patient. If minimal changes are present in the liver of a patient dying from some cause other than liver disease, such changes are usually not correlated with symptoms that may have been present. The liver biopsy has now stimulated an interest in even the smallest morphological abnormalities. When liver biopsy is done in a patient with complaints and biochemical evidences of liver disease, any histological deviation should be carefully studied. With this approach a sharper definition of the truly normal liver as it exists in the living human can be evolved. Intimately associated with the problem of definition is that of determining the relationship of the histological changes, if any, to either clinical symptomatology or biochemical abnormalities as measured in the laboratory. With the limitations of current investigative methods, to date there has been no positive correlation found between specific changes in the liver and either symptoms or biochemical changes.[14a, b] Since a consistent correlation of specific clinical findings with specific structural changes in the liver is lacking, the possibility must not be overlooked that extensive functional abnormalities may be present even with a completely normal appearing liver.

Finally, it can be stated that the liver biopsy offers a tremendous opportunity to the pathologist for the classification of liver disease on a rational basis. At present most classifications of liver disease are based on the end stages of hepatic disease only. Very little information is available concerning the early or intermediate stages of most liver diseases. It is not known how many of the acute liver diseases are capable, for example, of terminating in classic portal cirrhosis. A careful study of viral hepatitis may provide the opportunity to determine if there are permanent residuals of infectious liver disease. Efforts are now in progress to gather serial liver biopsy specimens in patients with acute viral hepatitis over a period of years, whether asymptomatic or not, to determine if morphological end stages of this disease are present and if they are progressive over a period of time. With this as a model it may be possible to establish an etiological rather than a morphological classification of liver disease. This worthwhile ideal may now become possible through the use of the liver biopsy and close collaboration of the clinician and the pathologist.

PULMONARY CYSTS

REPORT OF TWENTY-ONE CASES

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and
H. H. Bradshaw, M.D., Winston-Salem, N. C.

Pulmonary cysts, formerly believed to be relatively rare, are being seen with an increasing frequency coincident with improvement in methods of study of chest disease, mass survey roentgenograms, and the present facility of exploratory thoracotomy. Thus, many lesions that previously might have been treated as tuberculous cavitation, pulmonary abscess, or empyema are demonstrated to be pulmonary cysts. Because of the likelihood of serious complications and sequelae, recognition of pulmonary cystic disease and an appreciation of the place of surgery in its management are of considerable importance. An experience with 21 cases of pulmonary cysts treated surgically in the North Carolina Baptist Hospital for the period of 1943 through 1950 forms the basis of this report.

It is remarkable that, despite the present high degree of accuracy in the preoperative diagnosis of surgical chest diseases, pulmonary cysts are frequently misdiagnosed. In this present series, less than half were admitted through the outpatient clinic or other sources of reference with a correct diagnosis. Lung tumor, abscess, tuberculosis, empyema, bronchiectasis, and diaphragmatic hernia comprise the majority of mistaken impressions. The small surgical risk attendant to removal of these cysts, the preventive medical aspects of extirpation, and the likelihood of cure or improvement demands a greater awareness and more accurate diagnosis of these lesions.

Considerable confusion prevails in the literature regarding the nomenclature and classification of the various types of cystic lesions of pulmonary origin. Blebs, bullae, balloon cysts, pneumatoceles, and "honeycomb lung" are descriptive terms frequently encountered. Differentiation into acquired and congenital types is often labored. Although some consider abscess and cystic bronchiectasis under pulmonary cysts, neither specifically belongs to this category. Pathological confirmation is frequently hindered by morphological alteration affected by inflammation and intracavitary pressure. For more detailed consideration of the many aspects of these interesting lesions, excellent reviews are available.[1] The following classification is suggested:

Congenital Cysts	Acquired Cysts
A. Bronchogenic	A. Bullous emphysema
1. Pulmonary	B. Blebs
2. Mediastinal	C. Parasitic cysts
B. Alveolar	

Illustrative cases from this series of 21 patients, demonstrating the clinical characteristics of the most frequently encountered types of pulmonary cysts, follow.

From the Department of Surgery, Bowman Gray School of Medicine of Wake Forest College.

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REPORT OF CASES

CASE 1.—A 14-day-old boy, product of normal term gestation and delivery, was admitted in extremis, cyanotic, and with labored respiration. From birth cyanosis had been intermittent, and a chest roentgenogram taken on the second day of life showed large gas-containing spaces in the left chest, interpreted as diaphragmatic hernia. Laparotomy was performed at age 3 days but no diaphragmatic defect found. Respiratory embarrassment and mediastinal shift increased progressively, and the patient was transferred to the North Carolina Baptist Hospital. Roentgenograms showed multiple air-containing cavities in the left chest, with the heart markedly shifted toward the right (fig. 1).

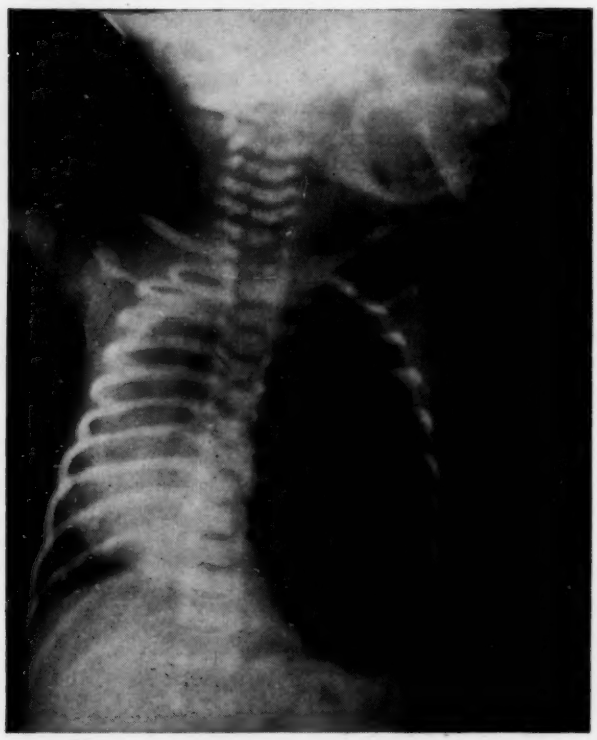

Fig. 1 (case 1).—Marked mediastinal shift resulting from multiple large bronchogenic cysts in left lung.

Because of his moribund condition, thoracotomy was deemed imperative for decompression of multiple tension cysts. This was carried out under ether anesthesia supplied by tight mask, through the posterolaterally resected left fifth rib. A large loculated cystic structure was found in the upper portion of the lung, which was devoid of fissures, lobes, or other usual landmarks. There was no mediastinal separation between the right and left chest, and it was possible to look directly into the right hemithorax. The right lung could not be seen and hence was believed to be either aplastic or atelectatic. The precarious condition of the patient made further exploration unwise. The cyst-bearing portion of the lung was simply excised in order to preserve as much functioning parenchyma as possible, and the small bronchiolar leaks were closed with suture ligatures. The postoperative course was complicated by recurrent pneumothoraces, which were controlled with thoracotomy suction. He was discharged on the 32nd postoperative day.

Pathological sections of the specimen showed multiple cysts of typical bronchogenic structure. To date (10 months) the infant has grown and developed normally, without pulmonary or respiratory sequelae. At age 6 months the left main stem bronchus would not admit a bronchoscope and bronchograms showed it to end abruptly, no branches being filled. The left bronchial tree was thus felt to be markedly deformed, perhaps partially aplastic.

CASE 2.—A male infant was admitted on his 10th day of life with a history of labored respiration and cyanosis, requiring oxygen constantly since birth. Gestation and delivery were normal. Chest roentgenograms taken on the first day of life were interpreted as showing a giant cyst in the right lung, and he was treated by thoracentesis and continuous oxygen until admission. Films taken on admission showed the mediastinum to be markedly shifted by multiple large air-filled cysts occupying the right chest and extending across the midline. Decompression of the cysts by inter-rib thoracotomy suction was attempted in order that the condition of the infant might be stabilized and hydration and nutrition improved before exploration. After 48 hours he failed to improve and exploration appeared advisable. This was carried out under endotracheal ether, through a posterolateral right fourth rib thoracotomy. The right middle lobe was found to be the site of multiple air-filled tension cysts, the upper and lower lobes being atelectatic but evidencing no cystic disease. Right middle lobectomy was performed, allowing the upper and lower lobes to expand completely. The postoperative course was uneventful, and the baby was discharged eight days later. He has appeared to be entirely normal for the short follow-up interval (three months). The resected middle lobe was found microscopically to consist entirely of multiple bronchogenic cysts.

CASE 3.—A 28-year-old woman was discovered on a routine chest roentgenogram to have a mediastinal mass. Two weeks later, asymptomatic and without significant related physical findings, she was admitted to the North Carolina Baptist Hospital. Roentgenograms demonstrated a smooth round opacity in the left middle mediastinum, measuring approximately 3 cm. in diameter (fig. 2). Exploration was undertaken through a left posterolateral sixth rib thoracotomy. A 3 by 4 by 5 cm. cystic structure was found between the pulmonary artery and the arch of the aorta, having no attachment to the visceral pleura or the lung. It was easily shelled from its bed after incising the parietal pleura. The postoperative course was uncomplicated, and she has remained well over the year since surgery. The external surface of the specimen was smooth and glistening, and it was filled with a mucinous substance. Microscopic sections showed the wall to be composed of smooth muscle and the lining to be columnar epithelium, confirming the diagnosis of mediastinal bronchogenic cyst.

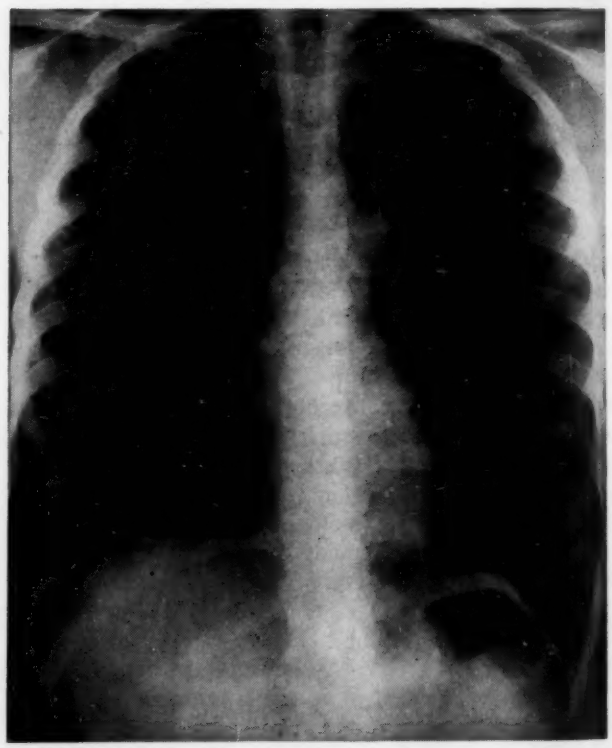

Fig. 2 (case 3).—Solitary asymptomatic bronchogenic cyst discovered on survey chest film.

CASE 4.—A 25-year-old woman gave a 15 year history of respiratory disease. Because of chills, fever, and productive cough, she was treated for pneumonia on repeated occasions. Persistence of cough led to sputum studies, which were negative for acid-fast bacilli, and she was advised that she had no serious pulmonary disease. Recurrent chills and fever and increasing cough

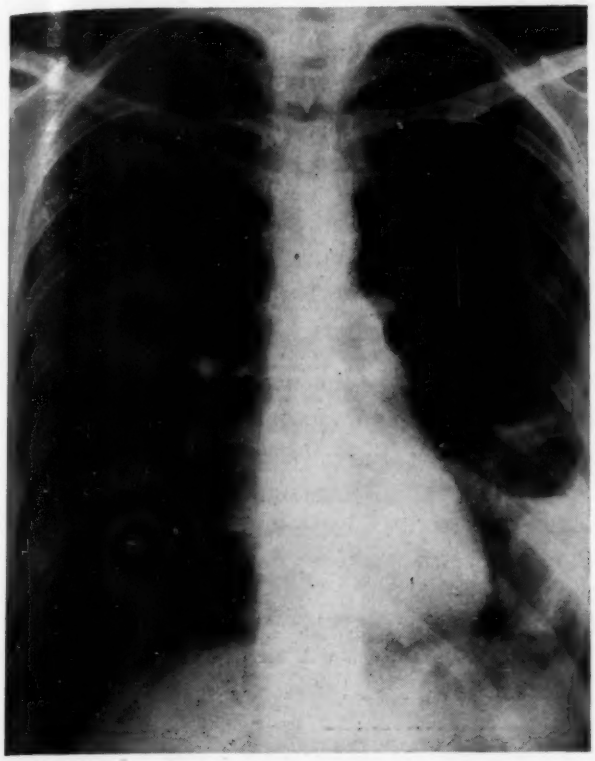

Fig. 3 (case 4).—Multiple infected bronchogenic cysts of left lower lobe.

and sputum brought her to this hospital. Roentgenograms disclosed an irregular cavity at the left base, with a fluid level (fig. 3). At exploration, many dense vascular adhesions were found binding the left lower lobe to the chest wall. A large cystic mass was palpable in the anteromedian basal segment, which was resected. The postoperative course was uncomplicated, and she has remained asymptomatic over a two year period. The resected segment contained a 6 cm. cavity, having multiple bronchiolar communications and filled with purulent fluid. Microscopic findings were typical of bronchogenic cyst, and the surrounding tissue showed secondary bronchiectasis.

CASE 5.—A 33-year-old man had persistent cough with occasional mucoid sputum over a period of 16 years before a "cavity" was discovered on a survey roentgenogram. He was hospitalized on this account in a tuberculosis sanitorium, where repeated sputum studies disclosed no tubercle bacilli, and he was transferred for consideration of exploration. Breath sounds were diminished in the right base posteriorly, and the roentgenogram demonstrated a cavity in the right lower lobe with a fluid level. Thoracotomy revealed numerous adhesions between the parietal pleura and the right lower lobe, which was "meaty" and noncollapsible. Right lower lobectomy was performed, complicated by some troublesome bleeding from an anomalous systemic artery in the inferior pulmonary ligament. Convalescence was uninterrupted, and he has remained well over the succeeding 18 months. A cyst 4 cm. in diameter, filled with thin greyish fluid, was found in the resected lobe, surrounded by numerous similar small satellites. Sections confirmed the diagnosis of multiple bronchogenic cysts.

CASE 6.—A 50-year-old diabetic man was admitted with a four year history of dyspnea, orthopnea, and cough productive of glairy mucoid sputum. Streaky hemoptysis was observed twice. Because of roentgen evidence of severe lung disease, he was told that nothing further could be done and was advised that he should move to Arizona. With progressive incapacitating dyspnea, he presented himself at this clinic. Roentgenograms showed the left hemithorax to be almost completely occupied by a large air-filled cyst, all remaining lung tissue being compressed into a narrow angle along the hilus (fig. 4). At thoracotomy the left lower lobe was found to be replaced by a giant cyst, which deflated on pressure. The lingula was involved to a lesser degree by a similar process. Left lower lobectomy was performed, and recovery was uninterrupted. He was greatly improved immediately, but the follow-up interval has been too short for adequate evaluation. The resected lobe was the site of a 14 by 12 cm. cavity, surrounded by multiple smaller similar spaces, all lined with alveolar mesothelial cells, and having multiple bronchiolar communications. The diagnosis was multiple bullous cysts.

CASE 7.—A 29-year-old man presented with a chief complaint of cough of 10 years' duration, occasionally productive of mucoid sputum. He was rejected by Selective Service in World War II because of a "spot on the lung." Soon thereafter he was studied at the North Carolina Baptist Hospital, where the diagnosis of lung cyst was made and thoracotomy advised. He refused operation and over the following four year period continued to experience cough, with increasing dyspnea. A sudden episode of severe left pleuritic pain followed by persistent soreness prompted his return. Roentgenograms on his second admission showed a large air-filled cyst in the left lower lung field, producing considerable mediastinal shift. At operation, the giant cyst was found to be attached to the diaphragmatic surface of the left lower lobe, from which it was easily separated. It was removed, and the patient has been well over the succeeding 18 month interval. Microscopic study of the specimen was not diagnostic, for the calcium-flecked fibrous wall lacked an epithelial lining or other significant morphological characteristics.

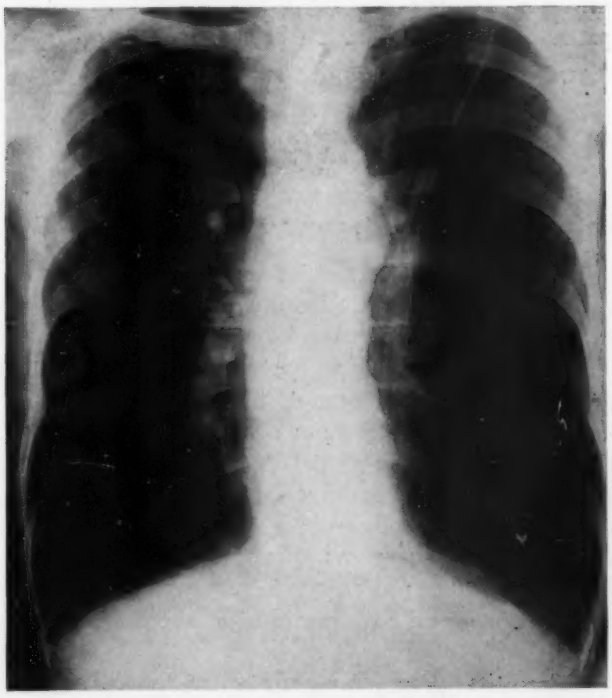

Fig. 4 (case 6).—Tension bullous cyst of left lower lobe.

COMMENT

This experience with 21 patients is representative of the problem of pulmonary cysts. Fifteen of these patients had bronchogenic cysts; three cysts were lined with alveolar epithelium, and three lacked sufficiently specific structure to be classified. Two bronchogenic cysts were mediastinal, 11 were intrapulmonary, and 2 were intramural, extramucosal esophageal lesions. Seven intrapulmonary bronchogenic cysts were multiple, and all

mediastinal cysts were solitary. All of the bullous emphysematous alveolar-lined lesions were multiple. Bronchogenic cysts occurred in younger persons, the two youngest patients (13 and 14 days) having this type. These infants represent, to our knowledge, the youngest reported cases of successful operative intervention in congenital pulmonary cysts. Gross [2] performed a pneumonectomy for this condition on a 3-week-old baby, and Burnett and Caswell,[3] a lobectomy on an infant of 15 days. The oldest patient in the series (50 years) had multiple emphysematous bullae.

The commonest preoperative complication was infection, and this was evident in 10 patients, 7 with bronchogenic cysts and 3 with lesions of indeterminate type. Tension phenomena occurred in four patients, two with bronchogenic cysts, one with emphysematous bullae, and one with a cyst of indeterminate type. This seems to be the commonest complication of bronchogenic cysts in infancy, while infection is more frequently seen in later years. Alveolar-lined cavities, probably because of less direct bronchial communication, seemed to have less probability for infection. The two mediastinal bronchogenic cysts were asymptomatic. Other pulmonary anomalies were encountered in three patients, all associated with bronchogenic cysts. An aberrant systemic artery in the right inferior pulmonary ligament was found in one patient, and in two the left bronchial tree was highly irregular. The most marked of these was the 14-day-old boy, case 1. The mistaken preadmission diagnoses in this series include: tumor, five instances; abscess, once; tuberculosis, twice; empyema, once; bronchiectasis, once; diaphragmatic hernia, once; and atelectasis, once. Nine patients were admitted with correct impressions. Six of the 21 patients were brought to attention by incidental survey roentgenograms.

The results of surgery in the treatment of pulmonary cysts are gratifying. In this experience there were no mortalities and the postoperative complications were negligible. This success is attributable to the fact that cyst extirpation is restorative surgery. Ventilation of lung tissue is increased by elimination of compression, infection, and sputum; pulmonary function almost immediately improves. The place of surgery in the management of the incidentally discovered chest lesion is emphasized in the treatment of pulmonary and mediastinal cysts. This realization assumes increasing importance with the growing popularity of chest roentgenogram surveys.

SUMMARY

Exemplary cases from a series of 21 patients with surgically treated pulmonary cystic disease are described.

2. Gross, R. E.: Congenital Cystic Lung: Successful Pneumonectomy in a 3-Week-Old Baby, Ann. Surg. **123**: 229-237 (Feb.) 1946.

3. Burnett, W. E., and Caswell, H. T.: Lobectomy for Pulmonary Cysts in a 15-Day-Old Infant with Recovery, Surgery **23**: 84-91 (Jan.) 1948.

MEDICINE VERSUS LAW: A PROPOSAL FOR SETTLEMENT

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Probably no subject in the law of evidence has received more attention than the problems of medical evidence in court. Most discussions of this subject deal with academic problems of opinion evidence. This is an attempt to delineate some of the problems that have arisen in the use of testimony of medical experts. Especially important is the availability of medical experts on the plaintiff's side in malpractice actions. Perhaps much of the difficulty results from a lack of appreciation, on the part of physicians and attorneys alike, of the problems of the other profession. In any event, the various solutions proposed have not brought about the reforms desired.

Attempts to present a picture of the "typical" lawyer as seen through the eyes of the "average" physician or vice versa are useless, for no such persons exist. One can, however, present the stereotypes freely acknowledged as such, a device not without some merit. To understand the sources of the resistance to cooperation on the part of members of both professions, it is necessary to understand which are grounded in fact and which in prejudice. Certainly no solution will be possible unless these internal resistances are taken into account. Although there are very real differences between the professions, some of the attitudes held by attorneys and physicians about each other result from misinterpretation of values deemed basic by each group. With the caveat that any such discussion must be oversimplified, an attempt will be made to describe both professions from an impartial position.

VIEW OF ATTORNEY AND PHYSICIAN

Ideally, the legal profession can be characterized as the protector of right, the guardian of order in society, and the representative of the ignorant, the misguided, and the injured, with justice the one goal and law the only means to this end. To engage in the practice of law is to be concerned with all the problems of living and to advise or represent persons or groups of persons who are in difficulty or attempting to avoid difficulty. The lawyer is likely to see the "seamy" side of life. Necessarily a partisan, the lawyer is almost constantly engaged in controversy, and his success is measured by his ability to prevail with his or his client's view of the case. Although one side must lose, the lawyer representing the losing side is often criticized for having taken the case in the first place. He may reply that all persons have a right to legal counsel and to trial by jury.

In the law, recovery is largely measured in money. Instead of "an eye for an eye," our present legal system

provides compensation in the money an eye is worth. Nevertheless, the law is criticized by some who contend that money does not mend all damage. Furthermore, the lawyer is said to be interested only in money. When unscrupulous members of the profession so conduct themselves as to confirm this prejudice, the whole profession suffers; indeed, the legal system itself loses stature. The medical profession views the human being with more restricted vision. Rather than dealing with conflicts between persons, the physician manages the problems of a single patient, at a time when he is ill or in danger of losing life itself. The patient turns to the physician not as an advisor but as a savior.

The physician is faced with one of three possibilities. The illness or injury may be one in which cure will be effected regardless of his skill or even of his attendance. Because of the state of medical knowledge, the illness may be one in which death or disability inevitably will ensue or one in which the physician's skill can determine the outcome. After years of practice the physician may be able to prognosticate more accurately, but he does not always know in which group a patient should be classified. Nevertheless, he must act and use his skill to the best of his ability. The physician is reminded constantly of the limitations of his profession, of the almost incomprehensible complexity of the human organism, and of health and disease. Disease knows no schedule. In medical practice, furious activity is followed by lulls of unpredictable length. Fatigue takes its toll in dulled senses. Frequently the physician either must see his patient when he is tired or must attempt—at peril—to delay until he is rested and more efficient.

The physician, too, has problems of compensation. He must be paid in money for his decisions, whether he charges by the visit or by the hour. He will usually adjust the fee on the basis of the difficulty of the case and the success of his skills. Unfortunately, the more difficult the case, the greater the fee, the more expensive the hospital bill, and the longer the patient is incapacitated and unable to earn his usual income. The patient may have feelings of both gratitude and resentment. When complete cure does not result, resentment must be directed at someone. If the patient has been injured, the resentment is directed toward the person causing the injury, but, if no external cause was present, resentment may be directed toward the physician in the form of a complaint about the size of the fee, or perhaps even as an accusation of malpractice. At this point an attorney is usually consulted. He sees only the end-result of the case and frequently is in no position to assess its merits. Urged by the client to recover compensation from someone, he knows that recovery, if obtained, will be a sizable amount of money.

PROBLEMS OF MALPRACTICE CHARGES

An ethical attorney faces a difficult situation. He must find out whether the case has merit. In the process of gathering facts, his mere questioning is construed as "building a case," and it is assumed that he has already decided the case is one of malpractice. The less ethical attorney is tempted by the size of the contingent fee to make a case regardless of its intrinsic merits. He may feel that all physicians carry malpractice insurance or that the physician can well afford the amount recovered. He may gamble on settlement of an unjustified case because of the possibility of unsavory publicity that the physician is anxious to avoid.

The word malpractice is almost synonymous with "quack," and its very mention will cause the physician to be wary. His reputation, his livelihood, his social position, and the entire medical profession are threatened when any suspicion of malpractice is aired. It is not for selfish motives alone that the medical profession is concerned with accusations of malpractice. Good medicine is practiced only when complete rapport exists between physician and patient, when there is implicit faith and confidence in the physician's ability to effect a cure. The patient cannot feel that his physician is negligent and yet be willing to place his life in his physician's hands. In short, malpractice charges are, to a physician, what disbarment proceedings are to a lawyer. Even if the charge is successfully defended, in each case, the profession has suffered and an individual is all but destroyed professionally. Certainly the public suffers in either event because of the lack of confidence in other practitioners that results. But it is the right of the injured party to be compensated, insofar as possible, for his injury. No physician or other professional person should be immune to suit for obvious wrong, but a procedure to compensate for wrong without vilifying the entire profession or causing unnecessary damage to the individual practitioner obviously would be desirable.

THE TRIAL PROCEDURE

It might be useful to view the procedural problems of litigation as the existing means of trying one's rights. Again the physician and attorney appear in sharp contrast. To the attorney, courtroom procedure is a situation for which he has trained specifically and for which he has spent years perfecting techniques. His task is to persuade a jury to believe his arguments in preference to those of his adversary; to say absolutely, "We find as a fact . . ." The physician, on the other hand, is entirely out of his element in the courtroom. Except on an academic or scientific level, controversy is unfamiliar to him. He deals in judgments as to probability, not with absolute fact; even a proved scientific fact has meaning only in relation to subjective impressions. To the physician, the courtroom means wasting valuable time to give a carefully restricted opinion, necessarily based on inadequate observation, for persons who cannot understand the details of the problem and who probably will not believe him anyway. His character, qualifications, veracity, or credibility may be attacked, and he may be subjected to indignities by a clever trial attorney. The physician is always at a distinct disadvantage in court, and he must neglect his patients during this time.

Because ethical and conscientious physicians are likely to be most resistant to appearance in court, the lawyer may be forced to accept any so-called expert who is willing to testify. "Professional witnesses," who will testify as experts on any medical specialty, are readily available in every jurisdiction. By implication, they cast an unfavorable light on both the legal and the medical profession. When the unscrupulous "professional witness" is pitted against an honest physician, too often the latter emerges second best. Since an active practicing physician has little opportunity to gain courtroom experience, he is not as "courtroom wise" as the "professional witness." It is unlikely that the conscientious physician will be willing to appear in court a second time. The legal profession consequently accuses the medical profession of protecting its members unreasonably by boycotting the courts.

An obvious result of discouraging honest testimony, of course, is the denial of the best possible help for the litigant. Annoyed at the unavailability of legitimate aid to his injured client, the lawyer resorts to use of the "professional witness." Thus a vicious circle develops consisting of the use of second-rate testimony, since the honest physician refuses to be involved and the honest physician's refusal to enter a courtroom controversy because testimony of a less honest member of his profession will be unfairly used against him.

PROPOSED SOLUTION

What are the remedies for this obviously unsatisfactory situation? In seeking a solution, we must determine (1) how the public can be assured the right to recover for injury, (2) how cases involving personal injury can be handled so expeditiously that recovery can be obtained at the time the patient needs the money, (3) how honest medical testimony can be assured, (4) how the legal profession can be assured that there will be no unreasonable protection or whitewashing of incompetent physicians, (5) how the medical profession can be protected from unwarranted attack and unsavory publicity by unjustified suits, and (6) how procedure can be modified to conserve the time of the physician as well as the court.

A plan of confidential procedure prior to filing an action could be postulated that would determine the merit of a case. If the case were found to be justified, a stipulation of fact would be prepared by a board instituted for examination of the medical facts. Such a board would have a rotating membership of both practicing physicians and attorneys approved by the medical society and the bar association. Panel members could be chosen from specialists in the subject matter under consideration. This preliminary procedure would need endorsement by the judiciary and agreement to abide by the stipulations arrived at if a case materialized and went to trial. If serious disagreement occurred at the preliminary hearing, resort could be had either to arbitration or to standard trial procedure, with only certified experts used as acceptable witnesses. The right of trial by jury would thereby be reserved for issues of fact, the preliminary procedure being a means of eliminating issue in appropriate cases.

A system of sanctions imposed by the court against the bar and by the medical licensure board and/or medical society against the medical profession would probably be required to enforce compliance with this procedure. Attorneys would be censured for filing an action after the impartial board had recommended against it. Physicians would be censured for refusing to give complete facts at the preliminary hearings. The whole procedure would be confidential, and unsavory publicity would be avoided. Since members of both professions are accustomed to speaking with undisputed authority, the confidential nature of the proceedings would avoid any threat to the unique position each profession enjoys with the public.

A pilot plan would be significant if devised and supervised by persons of undisputed competence who had no special ties in the selected jurisdiction. Some communities, notably the District of Columbia, have attempted to reach compromise agreements through joint committees of the medical and bar associations. Such a pilot plan would lend support to these local efforts.

Because of the importance of this question, the only feasible recommendation at this time would be for serious consideration of these proposals. If leaders in both professions, representatives of insurance companies, members of the judiciary, specialists in the academic fields involved, and representatives of the public all were given an opportunity to consult on this matter, a satisfactory solution could be evolved.

Hospital for Chronic Illness.

Florence Nightingale.—A rising standard of living, and the spread of "upper class" demands for comfort and of "upper class" habits of cleanliness through the community, have been the most important factors in the vast increase in health and length of life that has taken place since the middle of last century. Florence Nightingale is perhaps the key figure of that change. Aristocratic, religious, neurotic, and with a terrifying capacity for work, she realised that the physical comforts of food, space, cleanliness, and good manners that were available to her own class were the important things lacking in the handling of the sick and wounded soldier or the sick pauper. Since then public health has always included an interest in housing and working conditions and all that complex of social philanthropy and regulation which in our day has flowered into the "Welfare State."

Medical research in any ordinary sense has had little or nothing to do with this social revolution, which, I should guess, has been responsible for at least half the improvement in the expectation of life that has taken place in the last hundred years. Florence Nightingale never believed in bacteriology, and, though in due course the bacteriologists found good reasons for the benefit obtained by improving drains and supplying pure water, the whole process was well under way before the scientists had any influence whatever in administrative circles.

I have perhaps unduly stressed this point because I feel that when we are considering the social aspects of medicine we have to recognise that health depends on more than a regard for the bodily well-being of the individual as such.—Sir MacFarlane Burnet, M.D., The Future of Medical Research, *The Lancet*, Jan. 17, 1953.

STUDIES IN HUMAN SUBJECTS ON ACTIVE IMMUNIZATION AGAINST POLIOMYELITIS

1. A PRELIMINARY REPORT OF EXPERIMENTS IN PROGRESS

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WITH THE COLLABORATION OF

Major Byron L. Bennett, U. S. Army (ret.), L. James Lewis, Ph.D., Elsie N. Ward, M.A.
and
J. S. Youngner, Sc.D.

Investigations have been under way in this laboratory for more than a year, with the objective of establishing conditions for destroying the disease-producing property of the three types of poliomyelitis virus without destroying completely their capacity to induce antibody formation in experimental animals. The success of experiments in monkeys with vaccines prepared from virus produced in tissue culture and referred to briefly elsewhere [1] led to the studies now in progress in human subjects. It is the purpose of this report to present the results obtained thus far in the investigations in man. The voluminous detail of the preliminary and collateral experiments in animals will be elaborated on elsewhere. Before presenting the pertinent experimental data, I would like to review briefly the present state of the problem of immunization against poliomyelitis, and to discuss certain concepts of the nature of the disease as these bear on the studies here reported.

HISTORICAL BACKGROUND

Immunologic Complexity of the Poliomyelitis Virus.—Although the virus of poliomyelitis was first discovered by Landsteiner in 1909,[2] it was not until the report of Burnet and Macnamara [3] in 1931 that suspicion was aroused concerning the existence of more than one immunologic variety. Similar observations were described by Paul and Trask in 1933.[4] Little attention was paid to these very important observations, however, until considerably later. In the meanwhile the first attempts at immunization of man were made by Brodie [5] and Kolmer.[6] Were it not for the fact that these attempts made in the early 1930's were discontinued because the preparations employed were found unsafe for human use,[7] failure might have resulted for other reasons, one of which was the lack of more precise elucidation of the immunologic nature of the virus; this has been accomplished only recently.[8]

The surmise that more than one immunologic type of poliomyelitis virus exists was further supported by the studies of Lennette and Gordon in 1940 [9] and of Kessel and his co-workers [10] in 1946. Further confirmation of the results of these early investigations, and the firm establishment of the existence of at least two distinct types, was reported by Kessel and Pait [11] in 1948 and by Bodian, Morgan, and Howe [12] in 1949. Soon thereafter both groups of investigators [13] reported the existence of a third immunologic variety.

Because of the importance of the problem, a systematic program for immunologic classification of the poliomyelitis virus was organized under the Committee on Typing of the National Foundation for Infantile Paralysis. Through the cooperative effort of investigators at four universities, a study was undertaken to determine whether only three types exist, and to obtain preliminary information on the relative importance of the different immunologic varieties as a cause of the paralytic form of this disease.[8] On the basis of the findings in the study of the first 100 strains examined, it appears that the development of a procedure for the control of poliomyelitis by immunologic means need be concerned only with the three varieties of the virus that have been found thus far. They are now referred to as type 1 for those that are related to the Brunhilde prototype; as type 2 for those that resemble the Lansing strain; and as type 3 for those that resemble the Leon strain.

Pathogenesis and Immunogenesis of Poliomyelitis.—A great many significant observations that bear on the subject of pathogenesis and immunogenesis have been made in the course of numerous epidemiological and laboratory investigations in recent years. Rather than recount these completely or chronologically, it would seem to be more pertinent to the present thesis to begin with one of the most significant of the recent discoveries, not only to indicate the way in which earlier views were changed but to point up the influence of this discovery on the course of subsequent research.

The discovery by Enders, Weller, and Robbins [14] and of Evans and his associates [15] that the virus of poliomyelitis could be propagated in cultures of non-neural tissue not only made available new techniques for development of a source of virus for immunologic studies

This study was aided by a grant from the National Foundation for Infantile Paralysis.

From the Virus Research Laboratory, Department of Bacteriology, School of Medicine, University of Pittsburgh.

Owing to lack of space, all acknowledgments and some of the bibliographic references have been omitted from THE JOURNAL and will appear only in the author's reprints.

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but influenced profoundly and brought evidence to bear on the question of whether the poliomyelitis virus is strictly neuronotropic. This discovery supported the hypothesis that the virus may multiply in non-neural tissue and only thereafter be disseminated from the portal of entry or site of multiplication to the central nervous system. This hypothesis suggests further that the paralytic sequel of infection might be avoided if an antibody barrier could be created in the blood stream to intercept the virus before invasion of the central nervous system. Perhaps the first decisive experimental demonstration that this might be possible was the observation by Morgan [16] that antibody induced by subcutaneous vaccination of monkeys with live virus reduced the frequency of paralysis in animals subsequently inoculated intramuscularly with fully potent virus. Similar observations were made with a variety of strains in the course of the program on immunologic classification.[17]

Another significant observation was the finding of virus in the blood stream prior to the onset of paralysis both in experimental animals and in man, which was reported independently by Bodian [18] and Horstmann.[19] This, too, added support to the hypothesis that the viruses of poliomyelitis are not strictly neuronotropic. Bodian [20] promptly demonstrated that the virus could be intercepted before invasion of the central nervous system by passive administration of relatively low levels of antibody to cynomolgus monkeys and to chimpanzees that were then fed a virus that causes paralysis when given orally.

Further indication that viremia may represent a stage in the pathogenesis of central nervous system involvement in humans and that this may be prevented by the presence of a sufficient concentration of antibody in the serum was quickly forthcoming in the significant observation of Hammon and his associates.[21] They showed that relatively small amounts of antibody reduced the incidence and severity of paralysis if passively administered to children prior to the exposure or early enough in the incubation period.

Epidemiological Aspects of Immunity in Poliomyelitis.—The enormous amount of epidemiologic data that has accumulated over the years has been interpreted by most investigators as indicating that paralysis is the accidental occurrence in the course of a systemic infection that is widely experienced and is usually accompanied by the development of immunity rather than by central nervous system damage. Such observations made in the field as well as in the laboratory are in keeping with the opinion long held that the reduced frequency of paralysis with advancing years is due, in all likelihood, to the acquisition of immunity following nonparalytic infection early in life. The recent observation by Sabin [22] on the relationship of age of mice to the development of paralysis provides the basis for an attractive hypothesis to explain why crippling occurs less frequently and less severely in younger persons. Thus, it appears that, if immunity is not acquired in the early years when concomitant paralysis is less likely to occur, then the risk of paralysis some time in life is increased.

The reasonable immunologic explanation for the once mysterious epdemiological behavior of poliomyelitis is now well established. Only recently, however, has it been possible to begin a detailed and quantitative elucidation of the activities of the poliomyelitis virus under natural circumstances. Such systematic investigations can now be carried out through the application of Enders' tissue culture technique not only for the isolation of virus but also for the quantitative estimation of antibody for all three immunologic types. It is now possible to determine with relative ease not only the immunologic identity of the infecting virus but the frequency of the occurrence of antibody for the three virus types in various population groups. These methods have facilitated the progress of the studies reported here by providing a simple technique for determining the effect of active immunization on the level of serum antibody.

APPROACHES TO ARTIFICIAL IMMUNIZATION

Among the earliest reports on immunization of monkeys and then of man were those of Brodie [5] and of Kolmer [6] in the early 1930's. Their studies were conducted before precise knowledge regarding pathogenesis and immunologic complexity were available, and before there had accumulated the vast experience with the many strains that possess different pathogenic characteristics. Moreover, methods had not been developed for adequate purification of virus from suspensions of central nervous system tissue, nor were the dynamics of virus inactivation or modification well enough understood.

More than a decade later, Morgan [23] clearly demonstrated that a formaldehyde-treated suspension of central nervous system tissue from monkeys containing a type 2 strain of poliomyelitis virus did, after a rather rigorous schedule of immunization, induce the formation of appreciable quantities of antibody. She was also able to induce a measurable degree of resistance to intracerebral challenge in monkeys vaccinated repeatedly with similarly prepared type 1 virus.

Other investigators [24] in studies with mice and cotton rats confirmed the fact that preparations of type 2 virus that were noninfectious were still capable of inducing immunity in rodents. Thus, it would appear that materials devoid of demonstrable infectious activity for animals will immunize if given repeatedly in sufficient amount. This approach was extended by Howe,[25] who was able to demonstrate antibody formation in chimpanzees. In parallel experiments in six human subjects,[26] he observed the development of antibody that in most instances persisted over the observation period of six months; each child received 3.5 ml. of human gamma globulin followed by 3 ml. of vaccine.

20. Bodian, D. A.: Experimental Studies on Passive Immunization Against Poliomyelitis: II. The Prophylactic Effect of Human Gamma Globulin on Paralytic Poliomyelitis in Cynomolgus Monkeys After Virus Feeding, Am. J. Hyg. **56**: 78, 1952.

21. Hammon, W. McD.; Coriell, L. L., and Stokes, J., Jr.: Evaluation of Red Cross Gamma Globulin as a Prophylactic Agent for Poliomyelitis, J. A. M. A. **150**: 739 (Oct. 25) 1952.

23. Morgan, I. M.: Immunization of Monkeys with Formalin-Inactivated Poliomyelitis Viruses, Am. J. Hyg. **48**: 394, 1948.

26. Howe, H. A.: Antibody Response of Chimpanzees and Human Beings to Formalin-Inactivated Trivalent Poliomyelitis Vaccine, Am. J. Hyg. **56**: 265, 1952.

Another approach that has been suggested for inducing immunity is that of the feeding of attenuated living virus. Koprowski and his associates [27] have recently reported the results of studies in 20 human subjects fed a preparation of type 2 virus, which had been propagated in the central nervous system of rodents. In their studies, an immunologic response was induced and evidence found of virus multiplication in the gastrointestinal tract. The agent used for feeding was reported to be less pathogenic for the monkey than for rodents, but still caused paralysis when inoculated intracerebrally into the monkey.

It is evident from the foregoing that many observations made both in the laboratory and in the field have for a long time encouraged the expectation that immunization against poliomyelitis should be possible. The greater acceptability now of the idea that invasion of the central nervous system may be primarily via the blood stream [28] rather than primarily along neural pathways has increased the likelihood of such a solution. Moreover, the knowledge now available has reduced to reasonable levels the preliminary requirements expected for the performance of an immunologic method.

Although the objective to be achieved, in terms of serum antibody level, is more clearly defined and more reasonable of attainment, the question that still remains is how antibody formation may be induced in a practicable manner. The basic prerequisites are simple enough. These are first, a rich source of virus reasonably free of extraneous antigenic material and second, a method for destroying pathogenicity without completely destroying antigenic capacity. To these might be added a third, a means for enhancing antigenic activity if the richest source of virus available after treatment for destroying pathogenicity proves to be inadequate or borderline in its effectiveness. It is the purpose of this report to show how these objectives are being approached, and to present data on the degree of antibody response observed in man in the first experiments cautiously undertaken.

Virus of the three immunologic types used in these studies was derived from cultures of monkey testicular and monkey kidney tissue. The destruction of infectivity was accomplished by treatment with formaldehyde, and in some experiments emulsification with mineral oil employing the technique of Freund [29] was used for enhancing antigenic activity. It now remains for studies in progress (1) to establish the limits of reproducibility of the conditions for preparing noninfectious vaccines and (2) to determine the degree of persistence in humans of antibody induced by such preparations. Ultimately it will be necessary to test the ability of virus-neutralizing substances in the circulating blood that have been induced by vaccination to protect against the paralytic consequences of contact with the different immunologic types of poliomyelitis virus under natural circumstances. This will be necessary because of the possibility that invasion of the central nervous system by certain strains that occur in nature at different times may not be via the blood stream but by direct extension along nerve pathways, even though the weight of evidence has shifted from the latter to the former as a result of observations in recent years.

MATERIAL AND METHODS

Source of Virus for Vaccine.—The vaccines employed in these studies were prepared from virus propagated in roller tube cultures of two different tissues derived from monkeys. Monkey rather than human tissue was decided on for producing the virus for these experiments in human subjects because of the remote possibility that human tissue might occasionally be contaminated with such agents as the virus of infectious hepatitis that might conceivably propagate in cultures of human tissue. Even though the plan was to treat the culture fluids with formaldehyde to destroy the disease-producing property of the poliomyelitis virus, there could be no assurance that conditions for destruction of the latter, for which specific tests are available, would simultaneously destroy other agents of human disease for which no simple laboratory tests are available. Another consideration was the fact that methods had been worked out for producing the virus in reasonably high concentration employing relatively small amounts of monkey tissue.

Although testicular tissue was the first monkey tissue used for culturing the virus,[30] it appeared desirable to investigate other monkey tissues for comparison. Enders and associates [31] had employed such human sources as the foreskin, embryonic skin and muscle, the kidney, and the uterus. It seemed of interest, therefore, to explore cultures of monkey kidney and muscle, which are available in much larger supply than testicular tissue. The data in table 1 indicate the relative concentrations of virus derived from cultures of the kidney, testis, muscle, and liver of a single monkey. The advantage of the testicular cultures in yielding virus for long periods is offset by the greater abundance of virus in kidney cultures in the early days after virus inoculation. This example is presented to illustrate why the decision was made to use kidney rather than any of the other tissues in further studies on vaccines. The striking difference between cultures of kidney tissue and testicular tissue might well be due to the nature of the principal cell type, which is epithelial-like in kidney cultures and fibroblastic in testicular and muscle cultures.

TABLE 1.—*Infectivity Titer* of Fluids Harvested from Cultures of Various Monkey Tissues*

Culture Tissue	Days Following Inoculation						
	3	6	10	13	16	22	26
	Negative Logarithm						
Kidney	6.0	5.5	5.0	2.5	3.5	2.5	2.5
Testis	4.0	3.5	3.0	2.5	3.5	3.5	3.0
Muscle	2.5	3.0	2.5	2.0	2.5	2.0	2.5
Liver	2.0	0.1	0	0	0	0	0

* $TCID_{50}$ for monkey testis.

In the search for a fluid medium free of protein and still satisfactory for maintaining the viability of the tissues and for supporting virus multiplication, it was soon found that the chemically defined mixture no. 199 described by Morgan, Morton, and Parker [32] and first

28. Bodian, D.: Pathogenesis of Poliomyelitis (Don W. Gudakunst Memorial Lecture), Am. J. Pub. Health **42**: 1388, 1952.

29*b*. Freund, J.: The Effect of Paraffin Oil and Mycobacteria on Antibody Formation and Sensitization: A Review, Am. J. Clin. Path. **21**: 645, 1951.

used for similar studies by Rhodes and his associates [33] provided such a nutrient fluid. This mixture consists of a large number of amino acids, certain nucleic acid constituents, vitamins, and minerals, as well as other essential growth-promoting or growth-sustaining substances. Details of the use of this medium for cultivation of the three types of poliomyelitis virus in roller tube cultures will be elaborated on elsewhere. The roller cultures in which virus was propagated for the experiments to be described contained approximately 100 mg. of minced tissue with 4 ml. of nutrient fluid.

Selection of Strains.—For preparing the vaccines to be used in these investigations, strains were selected quite arbitrarily and principally on the basis of the regularity with which they could be propagated in relatively high titer in tissue culture. It is highly probable that substitutions will be made for certain of the strains now in use as further information is gathered in regard to the characteristics most desirable for inclusion in a vaccine.

The strains selected to represent types 1, 2, and 3, respectively, are known as the Mahoney, MEF-1, and Saukett strains. The Mahoney strain, which was isolated originally by Francis, was adapted to tissue culture from monkey central nervous system tissue. The MEF-1 strain, which was isolated by Schlessinger and Olitsky, was transferred to tissue culture from the spinal cord of paralyzed mice. The Saukett strain was isolated in this laboratory by direct inoculation of tissue culture with a fecal specimen from a patient paralyzed in 1950.

When inoculated into cynomolgus monkeys, these strains were found to have the following characteristics: The Mahoney strain is highly pathogenic by any route, whereas the MEF-1 and Saukett strains are essentially nonpathogenic except when given intracerebrally. When undiluted tissue culture fluids containing high concentrations of either of the latter two are injected by nonneural routes, paralysis will occur infrequently. Of the two, the Saukett strain produces the milder disease, even when given intracerebrally.

Infectious Titer of Fluids for Vaccine.—In the hope that others might repeat our experiments even before the final detailed reports of the various aspects of this work have been reported, the data on the infectious activity for tissue culture as determined in roller tubes containing fragments of monkey testicular tissue are reported here. This is but one measure that serves as an indicator of the concentration of virus in the starting material used for the preparation of vaccines. Table 2 contains such titration data on the virus pools involved in the vaccination experiments currently under way. These virus pools were prepared from a large number of small samples derived in the course of studies designed to learn how to produce the highest concentration of virus per unit volume of tissue culture fluid. Although they are not the most potent fluids that can now be produced, they have induced the effects to be described.

Destruction of Infectivity.—Prior to chemical treatment for destruction of infectivity, the culture fluids were first clarified by centrifugation and then stored in an electric deep freeze (at approximately –20 C). Before preparation for vaccine, the fluids were thawed, centrifuged until crystal clear, pooled, and then treated with formaldehyde.

On the basis of the results of numerous experiments, the details of which will be presented elsewhere, the decision was made to use 0.4% of a 37% solution of formaldehyde U. S. P. This reagent is commonly referred to as "formalin." Virus inactivation was allowed to proceed at the temperature of melting ice (approximately 1 C). The consideration that led to this decision was that at low temperatures the action of formaldehyde is relatively slow and might, thereby, be more selective in destroying infectivity without impairing too greatly the antigenic activity of the virus. It seemed a priori that the risk of overtreatment with formaldehyde might be reduced at low temperatures. With this as a starting procedure, a practicable and reproducible method for treatment of virus for vaccine could then be worked out. As will be illustrated, the concentration of formaldehyde employed was that required to destroy all traces of infectivity within a practicable period of time.

In the experiments here reported, the normal acidity of the formaldehyde solution used was neutralized in the usual way by the addition of solid magnesium carbonate, which was allowed to remain in excess at the bottom of the reagent bottle. One part of the neutralized solution of formaldehyde was added to 11.5 parts of balanced salt solution, and 5 ml. of this was added to 95 ml. of tissue culture fluid. Such mixtures are regarded as containing a 1:250 dilution of the U. S. P. solution of formaldehyde. The pools of each strain were treated separately and then distributed in 50 ml. quantities in vaccine vials and immersed in an ice water bath kept in the cold room, rather than in the cold room alone, merely to insure constancy of temperature (at

TABLE 2.—*Titration Data on Pools Containing Poliomyelitis Viruses* Used in Human Vaccination Studies*

Strain	Pool No.	Date of Pool Preparation	Dilutions †						Titer as Neg. Log. of 50% End Point
			10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}	10^{-6}	
Mahoney	7, 11 (T)	3/25/52	.....	24/24	29/41	16/40	3/32	0/5	3.8
MEF-1	15 (K)	6/20/52	.....	5/5	10/10	6/10	0/10	0/9	4.2
Saukett	10 (T)	3/27/52	17/20	14/25	2/15	0/16	0/4	...	2.4
Mahoney	25 (K)	10/23/52	.....	4/4	4/4	7/9	2/9	0/9	4.5
MEF-1	26 (K)	10/31/52	.....	8/8	6/6	8/8	4/7	1/6	5.2
Saukett	24 (K)	10/ 6/52	.....	4/4	13/13	10/13	1/12	0/12	4.4

* The viruses were propagated in cultures of monkey testis or monkey kidney and titrated in cultures of monkey testis.
The pools included fluids derived from several successive harvests of each set of cultures; many of the samples pooled together had relatively low titers. The letters in parentheses indicate tissues used for culturing the virus: T = testis, K = kidney.
† The numerator represents the number of cultures showing cytopathogenic change, and the denominator represents the number inoculated with each dilution.

approximately 1 C) for the period of treatment with formaldehyde. At intervals decided on in advance, the action of formaldehyde was arrested by the addition of approximately 1 ml. of a 35% solution of sodium bisulfite per 50 ml. of formaldehyde-treated fluid; the acid that results from this reaction was then neutralized by the addition of sufficient 1.0 N sodium hydroxide to return the pH to 7.4. The quantity of sodium bisulfite needed to neutralize the free formaldehyde was determined by means of a test described by Schryver and suggested to us by Dr. Joel Warren and Dr. Albert B. Sabin.[34] After treatment with sodium bisulfite, the preparations were then returned to the ice water bath for several weeks, until it had been established that storage in the ordinary refrigerator at 1 to 4 C did not impair infectious infectivity. Subsequently storage has been in the refrigerator at 1 to 4 C.

Mention should be made of the observation that different periods of treatment with formaldehyde were required for eliminating infectivity of the different preparations studied. It appears that the type 3 strain (Saukett) was the most sensitive in this respect, with the MEF-1 (type 2) and Mahoney (type 1) strains more resistant, in that order. Whether these observations mean there are qualitative differences among strains in their sensitivity to inactivation by formaldehyde or whether what has been observed is a function of virus concentration remains to be determined.

A series of experimental vaccines that had been subjected to different degrees of treatment with formaldehyde was prepared in the manner just described. After determination of which preparations were devoid of infectivity for monkeys, they were then ready for tests of antigenic activity in human subjects, to establish the limits of treatment with formaldehyde within which antigenic activity might still be present.

Safety Tests.—The first problem that had to be resolved before human subjects could be inoculated was the question of safety. It has been the consensus that tests for safety should include the intracerebral inoculation of monkeys. In all of the material employed for human beings, the absence of infectivity for the cynomolgus monkey was established in prior tests by the intracerebral inoculation of 0.5 ml. of fluid in 6 to 10 animals. As an additional safeguard, the only preparations considered satisfactory for use were those that had been exposed to the action of formaldehyde for at least 24 to 48 hours after the test just described indicated that infectivity had been destroyed. The fact that amounts of virus that produce paralysis when given intracerebrally are not paralytogenic when given intramuscularly or intravenously suggests that the intracerebral safety test may provide a more than adequate margin in certifying a given preparation as safe for use in human subjects.

Tissue culture methods have been developed for the detection of residual virus activity in the chemically treated preparations. Studies for correlating the results of tests for residual virus activity as measured in tissue culture and in the monkey are now under way. Until the relative sensitivity of the two has been determined, the number of monkeys used for establishing safety will be at least as great as that employed in the present investigations.

Reagents for Preparing the Emulsified Vaccines Used in Human Subjects.—The experience gained in studies in man on influenza virus vaccines* emulsified with mineral oil was utilized in preparing similar vaccines for studies on immunization against poliomyelitis. Experiments performed in the past three years in both animals and man have revealed that it is possible to avoid undesirable reactions at the site of inoculation of emulsified vaccines by the use of nonirritating reagents and by intramuscular administration of the inoculum. In the course of these studies it was found that when clinically recognizable local reactions occur, they are caused by certain constituents present in some batches of the crude emulsifying agent "arlacel A," the principal component of which is mannide mono-oleate. A way has been found by which these reactive impurities can be removed, and only such purified preparations were employed in these studies.

The mineral oil used in these experiments, known as "drakeol no. 6," is manufactured under conditions that satisfy the requirements for medicinal oils as established by the National Formulary. The preparation of purified emulsifying agent was mixed as a 3% solution in the mineral oil and sterilized by Seitz filtration. This was then mixed with equal parts of the tissue culture fluid for preparation of the emulsified vaccines.

Tests for Antibody in Human Serum Samples.—Blood was collected aseptically, and an effort was made to draw 10 to 20 ml. at each sampling to provide sufficient serum for repeat tests. The serum was then separated with sterile precautions and stored in the cold room at 1 to 4 C. Heating of the serum at 56 C prior to serologic testing was not done, since labile, nonspecific, antiviral factors were not encountered in tests in which heated and nonheated samples were compared.

Antibody determinations were made both in tissue cultures and in mice. Tests for types 1, 2, and 3 antibody were made in tissue cultures using virus strains that were selected particularly for their capacity to induce marked changes in cultivated cells. In some instances, tests for type 2 antibody were done in mice using strains of virus pathogenic for these species. Serial four-fold dilutions of serum, usually beginning with 1:4 dilutions, were mixed with equal volumes of virus suspension and inoculated either into culture tubes or intracerebrally into mice.

Fragments of monkey testicular tissue were used for the serologic test in tissue culture. The 0.5 ml. inoculum for each culture contained 100 50% tissue culture infecting doses ($TCID_{50}$) of virus in final mixture with each dilution of serum. After the addition of medium, each culture tube then contained 2 ml. of fluid. The method for preparing cultures for this purpose has been described,[35] but the medium employed and other details of procedure have been modified since the original report. The new details are to be presented elsewhere. In the exploratory phases of the serologic tests, two culture tubes were used for each serum dilution, but in

* A report of these studies is soon to appear in THE JOURNAL.

almost all instances reported here repeated tests were done so that the results represent an accumulation of four or more cultures for each dilution. The same virus pool was used as antigen throughout and at the same dilution.

TABLE 3.—*Number of Subjects in Vaccination Studies in Progress, January, 1953*

	Experiment No.	No. of Subjects
D. T. Watson Home	1, 2, 3, 5	52
	7	18
	8	28
Total		98
Polk State School	1	16
	2	16
	3	16
	4	15
Total		63
Total in all experiments		161

Pre- and postvaccination serum samples were always tested simultaneously, and when later blood samples were available an early blood sample was always tested together with the later one, so as to allow the results of tests of newly drawn serum samples to be related to previous ones tested at an earlier time. In some instances four and five serum samples drawn at different intervals in relation to vaccination were tested simultaneously. In this way, factors that might be attributable to inherent variations in tests carried out on different occasions were reduced or eliminated. Titers are expressed in terms of dilution of serum that was added to the virus before inoculation, either into the culture tube or the mouse, and are expressed as the 50% end point.

Each time a serologic test is performed, whether in tissue culture or in mice, a standard reference serum of high titer is included along with a sample of serum containing no antibody; these are in addition to the usual controls, which include the virus titration and, in the case of the tissue culture test, a group of uninoculated cultures. Tests done in mice were carried out with 32

TABLE 4.—*Significance of Serum Antibody as Indicator of Previous Infection with a Particular Type of Poliomyelitis Virus*

	Patient			Antibody Titer in 1952		
Year of Paralysis	No.	Age in 1952, Yr.	Virus Type in Feces	Type 1	Type 2	Type 3
1950	W-73	13	3	0	0	512
	W-74	11	3	0	0	512
	W-40	18	1	512	0	512
1951	W-13	6	1	512	0	0
	W-21	2	1	256	0	0
	W-31	4	1	512	0	0

LD_{50} (50% lethal doses) of virus, and 0.03 ml. of each serum-virus mixture was inoculated intracerebrally into each of eight mice.

HUMAN SUBJECTS

In extending to man studies on vaccination performed in laboratory animals, tests on more than a few individuals had to be anticipated. The first persons to participate in these studies were patients paralyzed in recent years by a poliomyelitis infection and who were in residence at the D. T. Watson Home for Crippled Children, Leetsdale, Pa. In addition to patients who had recovered from paralytic poliomyelitis, there were others who were in residence at the Watson Home for such diseases as arthritis, spastic paralysis, and a variety of congenital deformities. After the initial investigations were under way at the Watson Home, additional studies were undertaken at the Polk State School, Polk, Pa.

The numbers of subjects involved in the several experiments under way are indicated in table 3. Of the group of 98 patients at the Watson Home, 51 are participating in studies involving aqueous vaccines inoculated intradermally, and 27 are involved in studies on emulsified vaccines given intramuscularly. All of the 63 individuals at the Polk State School have been given emulsified vaccines intramuscularly.

Because many persons at all age levels have antibody to one or more of the three types of poliomyelitis virus, and because such persons as well as those with no antibody at all have to be used in studies on immunization,

TABLE 5.—*Frequency of Antibody to Only One Immunologic Type in Serum of Seventy-Nine Patients with Paralytic Poliomyelitis*

Year of Paralysis	No. of Patients	No. with Antibody for One Type			No. with Antibody for More Than One Type
		Type 1	Type 2	Type 3	
1945	1	1	0	0	0
1948	1	0	1	0	0
1949	3	3	0	0	0
1950	12	1	0	9	2
1951	29	21	0	1	7
1952	33	16	5	2	10
Totals	79	42 (70%)	6 (10%)	12 (20%)	19

it would be well to explain the significance of the presence of serum antibody as an indicator of previous infection.

Immunologic Status of Recently Paralyzed Patients.—Data are presented in table 4 showing the results of immunologic studies in six patients one to two years after their acute paralytic infection. In this group virus had been isolated from fecal samples collected shortly after the onset of paralysis. It is of interest to note that, in the three patients who had poliomyelitis in 1950, type 3 virus was isolated in two instances, and in both instances antibody for the type 3 virus only was found in the serum two years later. In the one patient from whom type 1 virus was isolated in 1950, antibody for both type 1 and type 3 virus was found in 1952. It is probably correct to conclude that the type 1 antibody resulted from the type 1 infection that occurred in 1950 when the type 1 virus was isolated. It is impossible to say, however, whether or not the type 3 antibody resulted from infection that also occurred in 1950 when virus of this type was in circulation, or at some previous time, or perhaps subsequent to 1950. Of the three patients who were paralyzed in 1951 and from whom the type 1 virus was isolated at that time, antibody for the latter virus only was found in 1952, and there was no demonstrable antibody for either the type 2 or type 3 virus.

The foregoing facts illustrate that the neutralizing antibody response that persists in naturally infected human subjects is type specific, and that it is still present at fairly high levels for at least one or two years after a clinically recognizable infection. It is of further interest that the presence of antibody for one particular type, in a paralyzed person whose serum is devoid of antibody for any other type, probably indicates the immunologic nature of the infecting virus.

Complete data on tests for antibody for the three immunologic types are available in a group of 79 recently paralyzed persons. Table 5 contains a summary indicating (1) the year when paralysis occurred and (2) the antibody status in 1952. Of the 79 patients, 60 have antibody for only one immunologic type; only 19 possess antibody for more than one type.

It would appear from these data that in the area of Western Pennsylvania from which these patients were drawn, the type 3 virus was more prevalent in 1950 and

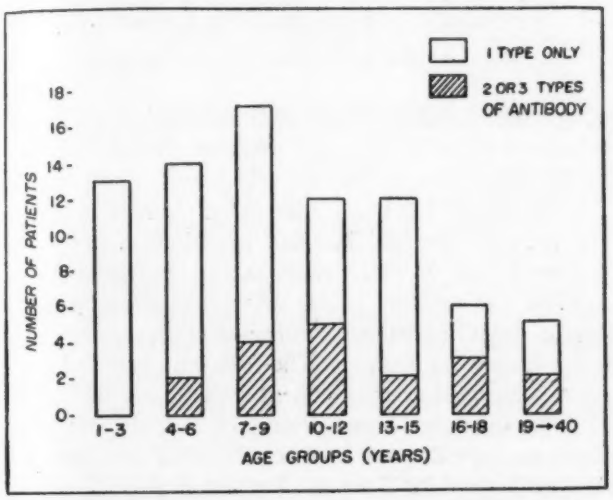


Fig. 1.—Age distribution and number of persons with serum antibody for one or more types of poliomyelitis virus among 79 patients with paralytic poliomyelitis.

the type 1 virus in 1951, and that all three types were in circulation in 1952. While it is evident that types 1, 2, and 3 viruses have caused paralysis in recent years, it appears that, in the period for which data are available, type 1 has been the most prominent.

Where antibody for more than one type is present, it may be presumed that nonparalytic infection preceded the paralytic attack caused by one or another of the poliomyelitis viruses. Table 6 contains the ages of those with antibody to more than one type, and the immunologic types for which their serum possesses some antibody. As might be expected, the age distribution of those with antibody for more than one type is somewhat higher than in those with antibody for only one type. This is illustrated further in figure 1, which shows not only the age distribution in this particular group of recently paralyzed patients but the frequency with which antibody for one or more than one type was encountered in relation to age.

Poliomyelitis is not a single disease, since it can be caused by any one of three immunologically different viruses. Therefore, persons who have had paralytic poliomyelitis are considered satisfactory for studies on active immunization. From the immunologic viewpoint, these individuals are similar to others without previous history of paralytic poliomyelitis, since there are many persons who may have at one time or another been in-

TABLE 6.—*Patients with Paralytic Poliomyelitis Who Possess Serum Antibody for More Than One Immunologic Type*

Year of Paralysis	Patient No.	Age in 1952, Yr.	Serum Antibody * vs. 100 $TCID_{50}$ of Virus		
			Type 1	Type 2	Type 3
1950	W-10	34	+	+	−
	W-40	18	+	−	+
1951	W-16	16	+	+	+
	W-12	10	+	+	+
	W-32	17	+	−	+
	W-34	14	+	−	+
	W-35	11	+	−	+
	W-2	11	+	−	+
	W-23	7	+	−	+
1952	W-86	13	+	+	+
	W-90	10	+	+	+
	W-208	9	+	+	+
	W-206	4	+	+	+
	W-117	16	+	+	−
	W-139	5	+	+	−
	W-88	40	+	−	+
	W-200	11	+	−	+
	W-85	9	+	−	+
	W-201	9	−	+	+

* + = presence of antibody; − = absence of antibody.

fected with one or two of the three types of virus without becoming paralyzed. Individuals whose blood is devoid of antibody for any one virus type can not be regarded as immune to the disease because they have not experienced infection with all three types.

Immunologic Status of Subjects Without Prior History of Poliomyelitis.—The age distribution in the 63 subjects at the Polk State School, who are included in the experiments in progress, is shown in table 7. Data available indicate that a high proportion possess antibody for one or more virus types even though these subjects have not had paralytic poliomyelitis. The fact that many more have antibody for more than one type as compared with patients at the Watson Home is

TABLE 7.—*Age Distribution of Sixty-Three Subjects at the Polk State School*

Age Levels, Yr.	No. of Subjects	Age Levels, Yr.	No. of Subjects
4-6	6	19-21	4
7-9	10	22-24	4
10-12	9	25-27	5
13-15	7	28-30	6
16-18	12		

probably a reflection of the higher age level in the Polk group. It is of further interest that clinically recognizable poliomyelitis has occurred at the Polk State School only once in the past 35 years, and that was in the late fall of 1951. At that time six cases occurred, one of which terminated fatally. This represented an attack rate of approximately 180 per 100,000. At the time these cases occurred, there was no increased incidence of illness suggestive of nonparalytic poliomyelitis.

EXPERIMENTAL PROCEDURES AND RESULTS

The principal purpose of the experiments to be described was to determine whether or not the experimental vaccines that were made could induce antibody formation in human subjects. In the initial explorations,

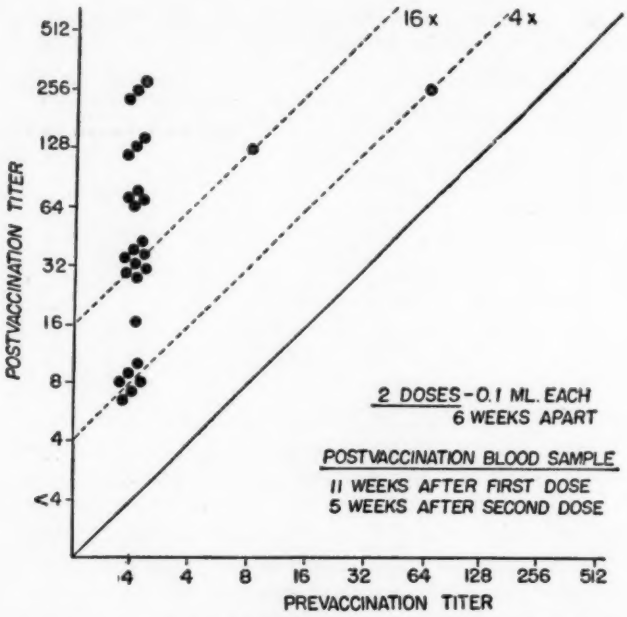


Fig. 2.—Serum antibody titer before and after intradermal inoculation of 27 human subjects with type 2 poliomyelitis vaccine that had been treated with formaldehyde (experiment W-5). The titer is expressed in terms of the dilution of serum that was added to the virus before inoculation, and is expressed as the 50% end point.

small doses of aqueous vaccines were inoculated intradermally. From the studies completed thus far, the indications are that only the type 2 preparation then available was effective when administered in this way. Later experiments were performed with experimental vaccines emulsified in mineral oil and inoculated intramuscularly. In these studies it was found that antibody for all three types was induced.

Since the conditions for destroying infectivity without completely destroying antigenicity were not known in advance, several experimental vaccines were prepared and were tested for antigenic effectiveness in human subjects inoculated with the dose and in the manner indicated. The variables under test, in terms of the extent of formaldehyde treatment of the different virus pools, are indicated in table 8. Sufficient time has not elapsed for titrating antibody in all serums that have already been collected, particularly in the more recent experiments. However, the immunologic results available to date will serve to indicate the trends observed thus far.

Although the primary objective of these studies was to determine whether or not the preparations selected on the basis of their safety for animals still retained antigenic capacity, another purpose was to obtain information in answer to the question of safety for human subjects. It is desired to state at the very outset that in none of the 161 persons involved have there been any signs of illness that could be attributed to the inoculation. Among subjects who received vaccine with mineral oil adjuvant, there have been no untoward local reactions. In subjects inoculated intradermally with the aqueous preparations an area of erythema and edema was observed at the site of inoculation, varying in size from a few millimeters to 35 to 40 mm. in diameter. It first appeared about 8 hours after inoculation and lasted as long as 48 hours in some instances. In the majority, the reaction began to fade after 24 hours.

TABLE 8.—*Variables Relating to Treatment of Tissue Culture Fluids with Formaldehyde**

Virus Type	Strain	Pool No.	Monkey Tissue Used	Days in Melting Ice			
Type 1	Mahoney	7-11	Testis	7	10	13	17
2	MEF-1	15	Kidney	10	13	17	21
3	Saukett	10	Testis	10	13	..	..
Type 1	Mahoney	25	Kidney	15	21	..	..
2	MEF-1	26	Kidney	13	15	21	..
3	Saukett	24	Kidney	6	7	8	..

* 1:250 dilution of "formalin" (37% solution of formaldehyde, U.S.P.).

1. *Aqueous Vaccines Inoculated Intradermally.*—The subjects involved in these experiments had been paralyzed, one or more years earlier, by acute poliomyelitis. The vaccines employed were made from tissue culture fluids treated with formaldehyde, as indicated in the section on methods. The following pools of each strain were used after treatment with formaldehyde for 13 days: for type 1, pools 7 and 11-T of the Mahoney strain; for type 2, pool 15-K for the MEF-1 strain; and for type 3, pool 10-T for the Saukett strain.

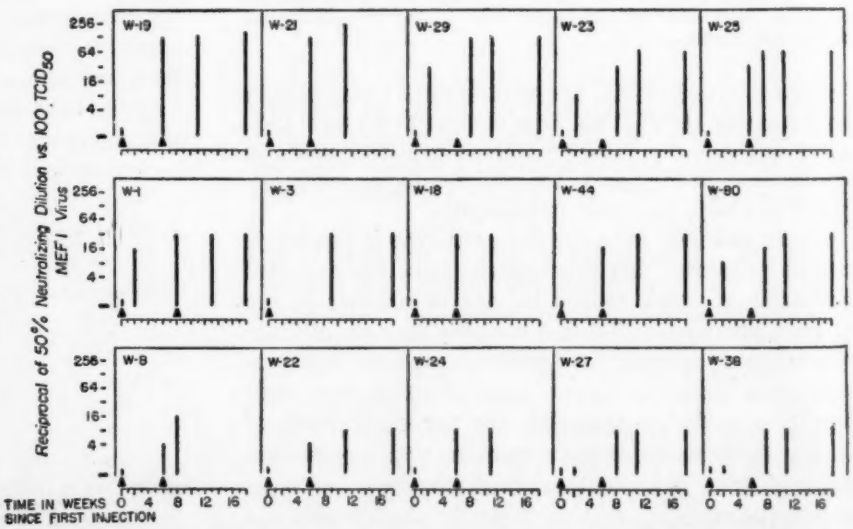


Fig. 3.—Antibody titers before and at intervals after vaccination of human subjects with type 2 poliomyelitis vaccine. The vaccine was given intradermally in doses of 0.1 ml.; it was prepared from MEF-1 pool 15 and treated with formaldehyde for 13 days at 1 C. The triangles indicate the dates of inoculation (experiments W-2 and W-5). This is to illustrate the effect of the first of two intradermal injections.

In the experiment designated W-2, 0.1 ml. of each type was inoculated into three separate sites on the volar aspect of the forearm. Six weeks after the first in-

oculation a second dose of vaccine was given. This part of the study was designated as W-5, and the types 1, 2, and 3 fluids selected for this inoculation had been treated with formaldehyde for 10, 13, and 10 days respectively. Blood samples were obtained at intervals before and after the first and second doses; serologic data for type 2 antibody are available in many subjects for intervals up to four and a half months after the first dose. Blood samples six months after the start of the experiment have been drawn for testing. Complete information is available only for the blood samples taken 11 weeks after the first dose, or when considered in relation to the reinoculation, 5 weeks after the second dose. These data are presented in the figures and tables that follow.

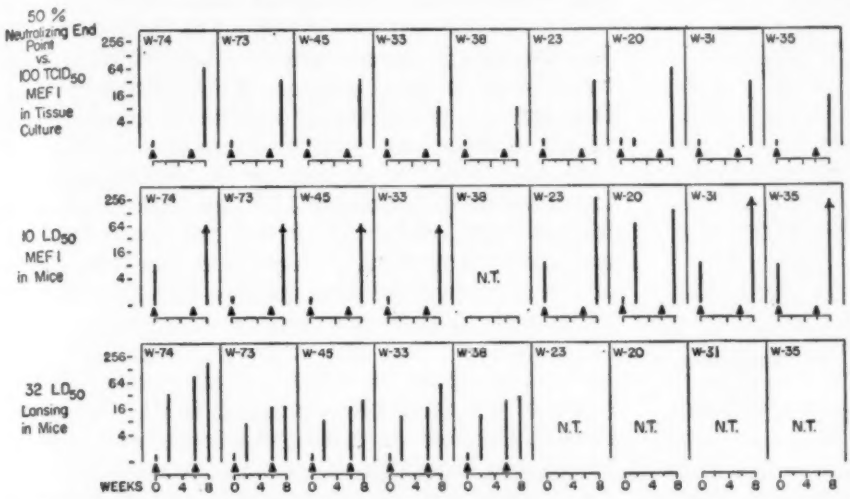


Fig. 4.—Comparison of antibody titers in tissue cultures and in mice tested with two different antigens. These subjects, from experiments W-2 and W-5, were vaccinated with 0.1 ml. The triangles indicate the dates of inoculation (experiments W-2 and W-5).

Antibody Response to Type 2 Vaccines Formaldehyde-Treated for 13 Days: Summarized in figure 2 are the antibody titers for the type 2 virus in 27 subjects who were inoculated intradermally with 2 doses of 0.1 ml. each, given six weeks apart. The postvaccination blood samples here recorded were taken in the 11th week after the first dose, or the 5th week after the second dose. Each symbol represents one individual and indicates both pre- and postvaccination antibody titers by its position in relation to the horizontal and vertical coordinates. In 25 of the 27 subjects no type 2 antibody was demonstrable before vaccination, and in all instances the titer rose to levels of from 1:8 to 1:256. The two who had antibody before vaccination also responded with a rise in titer. It is evident from the position of the symbols in relation to the diagonal lines that a four-fold or greater rise in antibody titer developed in all 27.

In view of these rather unexpected findings, it was of interest to examine the earlier serum samples that had been collected as well as the later ones to determine, if possible, (1) the effect of the first of the two intradermal injections; (2) how soon the antibody rise could be detected; and (3) the degree of its persistence. The data available to date relative to these questions are summarized in figure 3. In only 15 subjects have tests been completed on serum samples taken following the first dose. It is clear that a substantial part, if not all, of the antibody response occurred within six weeks of the first inoculation. In eight persons from whom serum samples were taken two weeks after the first dose, tests have been done, and in six antibody had made its appearance by this time; in two none was yet demonstrable by the serologic method employed. In the latter two instances it appears that the second inoculation may have brought about an antibody increase that the first dose failed to accomplish, although this is not certain since there is no information on the serum taken at the time of the second dose. In most instances the data suggest that little or no change followed the second dose, although there is also the impression that the second dose may have had some effect.

In 11 of the 15 individuals included in figure 3, antibody titers are available four and a half months after the initial inoculation, and in none is there any indication as yet of fall in the level of antibody induced by vaccination. Also in figure 3 is included the data for subject W-3, who received only one inoculation. It is of interest to note that two serum samples taken at 9 and 18 weeks after the first inoculation both show the same level of antibody. Complete information will be had, in due course, for all of the subjects in this experiment; tests for persistence will be continued as long as possible.

In order to assess further the significance of the results just presented, tests for antibody in a limited number of subjects have been made not only in tissue culture but in mice as well. In the latter, two different indicator viruses have been used, the MEF-1 and Lansing strains.

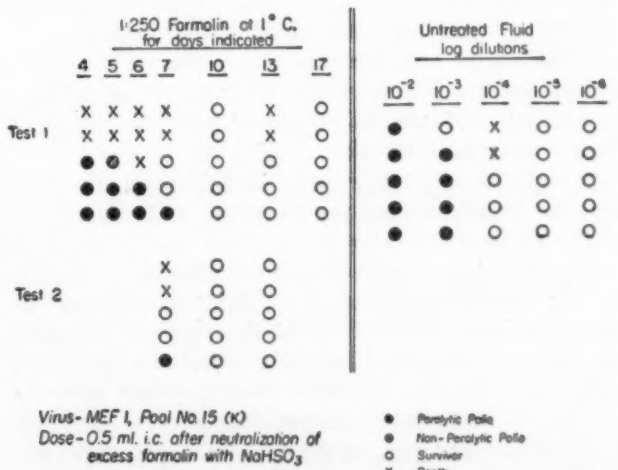

1:250 Formalin at 1° C. for days indicated
4 5 6 7 10 13 17
Test 1
Test 2
Untreated Fluid log dilutions
10-2 10-3 10-4 10-5 10-6
Virus - MEF I, Pool No. 15 (K)
Dose - 0.5 ml. i.c. after neutralization of excess formalin with NaHSO3
Paralytic Polio
Non-Paralytic Polio
Survivor
Death

Fig. 5.—Results of infectivity tests in cynomolgus monkeys with MEF-1 tissue culture fluid used for inoculation of humans.

When a small dose of MEF-1 virus (10 LD_{50}) was used for the antibody test in mice, there was some suggestion (fig. 4) that (1) a low concentration of antibody may have been present in prevaccination serum samples in four of the eight subjects so studied and

(2) that the values for postvaccination antibody titers are greater than those determined in tissue culture, in which a larger quantity of virus was used for the serologic test. In six instances no end point was reached in the highest dilution of the postvaccination serum tested. When the customary quantity of Lansing virus was used

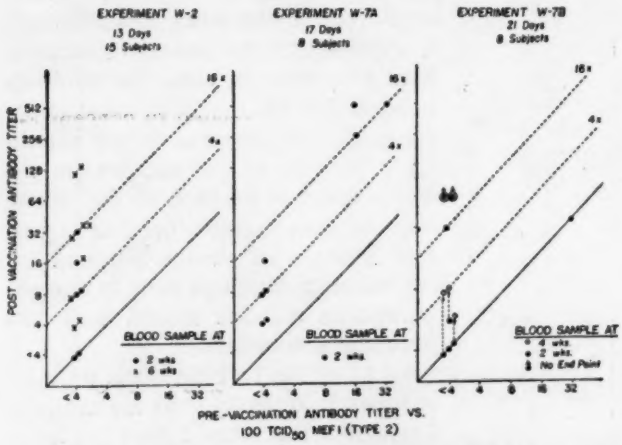


Fig. 6.—Antibody response in human subjects inoculated with vaccine prepared from MEF-1 pool 15 and treated with formaldehyde at 1 C for 13, 17, and 21 days. The excess formaldehyde was neutralized with sodium bisulfite. A single dose of 0.1 ml. was given intradermally, and blood samples were taken two, four, or six weeks afterward (experiments W-2, W-7A, and W-7B).

for the neutralization test (32 LD_{50}), there was no detectable antibody in the prevaccination serum sample of the five subjects so studied, and the gradual increase in antibody titer at intervals after the first dose, and perhaps even after the second dose, is indicated by the data summarized in the lower portion of figure 4. These comparisons serve to indicate that the antibody rise is real and is demonstrable repeatedly by different methods.

The observation that the numerical value for antibody titer estimated in the tissue culture system is somewhat lower than that determined in mice should be emphasized. This is probably due, in part, to the larger number of virus units employed in the serologic test; nevertheless, it suggests that the results of the tissue culture test are a conservative measure of the quantity of antibody induced, as compared with the results of similar tests done in mice.

Results of Infectivity Tests in Monkeys: In order that the significance of the foregoing findings may be evaluated in relation to the material inoculated, data are presented in figure 5 showing the infectious activity, for the cynomolgus monkey, of fluids from which the type 2 vaccine was derived. In this figure is indicated the fate of individual animals inoculated intracerebrally with samples of MEF-1 tissue culture pool no. 15, treated with formaldehyde for different intervals. It will be recalled that, on the days indicated, the excess formaldehyde was neutralized with sodium bisulfite. When such fluids were inoculated intracerebrally, not all of the animals could tolerate the concentration of the chemicals contained in these mixtures, and some succumbed shortly after inoculation. In some instances the symbol for death in the chart also refers to deaths not due to poliomyelitis that occurred before termination of the 30 day observation period. The solid black symbols indicate that paralytic poliomyelitis occurred; the one symbol with the shaded area indicates that no clinical signs of infection were observed in life, but histological evidence of nonparalytic infection was observed when the spinal cords were examined at the end of the 30 day observation period.

The vaccine used for inoculation of the human subjects involved in experiments W-2 and W-5 had been treated with formaldehyde for 13 days. From the data in figure 5, it would appear that this preparation was devoid of infectivity for the cynomolgus monkey, at least when tested in the number of animals indicated. It is noteworthy that on the 10th day of treatment with formaldehyde, virus activity was not detectable and may have disappeared, perhaps as early as the eighth or ninth day. It would seem unlikely, therefore, that the effects observed in the human subjects were due to residual infectious virus, and certainly not to any virus activity that could be detected by intracerebral inoculation of the cynomolgus monkey. It was of further interest, therefore, to determine whether or not fluids treated with formaldehyde for longer intervals, i. e., 17 and 21 days, were still antigenic when tested in human subjects. This was done in experiments W-7A and W-7B.

Influence of Duration of Formaldehyde Treatment on Antigenic Activity of Type 2 Vaccines: Data on the antigenic activity in man of type 2 vaccine from MEF-1 pool 15-K treated with formaldehyde for 13, 17, and 21 days are summarized in figure 6. Information for this chart is derived from the results in experiments W-2, W-7A, and W-7B. Data from W-2 are the same

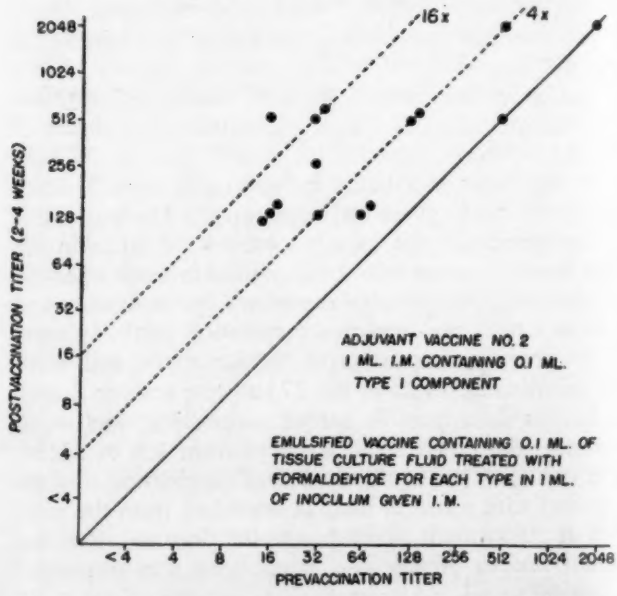


Fig. 7.—Antibody response to type 1 poliomyelitis virus in human subjects inoculated with vaccine containing all three immunologic types of poliomyelitis virus that had been treated with formaldehyde (experiment P-1). The titer is given in terms of the dilution of serum that was added to the virus before inoculation, and is expressed as the 50% end point.

as that contained in figure 3 for the 15 subjects in whom antibody determinations are known following the first dose; in some the two week postvaccination blood sample was tested, and in others only the six week level was determined. Nevertheless, the data for the 15 sub-

jects inoculated with the fluid treated with formaldehyde for 13 days are charted for comparison with the 8 subjects inoculated with fluids treated for 17 days and the 8 subjects inoculated with fluids treated for 21 days. The dose in each instance was 0.1 ml. inoculated but once and administered intradermally. Results of sero-

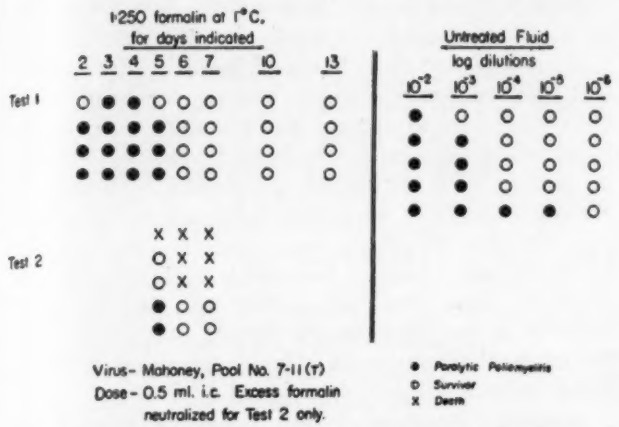


Fig. 8.—Results of infectivity tests for cynomolgus monkeys of Mahoney (type 1) tissue culture fluid that was used for inoculation of humans (experiment F-17).

logic tests only two weeks after vaccination are available at this time for subjects in experiments W-7A and W-7B. In the case of a few in experiment W-7B, four week postvaccination titers are also available. Where both have been determined, the results at two and four weeks are joined together by a dotted line or encircled if the result was the same in tests of both samples.

Although these data are too few to permit conclusion regarding the question of the relative degree of antigenic effectiveness in the human subject of the three preparations compared, it does appear possible to say that even after formaldehyde treatment of MEF-1 pool 15 (K) for 17 and 21 days, some degree of antigenic activity in the human subject is still present.

Comments on Results of Studies with Aqueous Vaccines.—In experiments of the kind just described, it is necessary to be certain that the immunologic changes attributed to vaccination are not caused by natural infection in the populations under study. It was for this reason that a group of controls was used to test this factor, and the results of studies in this group show no indication that rises in type 2 antibody occurred in this population within the interval of observation.

In concluding these remarks about the experiments on intradermal inoculation with preparations treated with formaldehyde, it is desired to point out that the very distinct rise in antibody that occurred following intradermal inoculation of the type 2 preparation was not paralleled in the subjects similarly inoculated with the types 1 and 3 preparations employed at the same time. The type 1 preparation that had been treated with formaldehyde for 10 days (Mahoney pools 7, 11) exhibited some antigenic activity in many subjects; however, the serologic tests have not been repeated in all instances and, therefore, are not ready for presentation at this time. There was no indication of any antigenic activity in the type 3 fluid that had been treated with formaldehyde for 10 days. The tentative conclusion that has been drawn is that the effectiveness of the type 2 (MEF-1 pool 15-K) preparation may be related to the presence of a greater concentration of virus in the starting fluid before treatment with formaldehyde, and that this may have been due to the fact that this pool was derived from cultures of kidney rather than testicular tissue. The latter was used in preparing the types 1 (Mahoney 7, 11-T) and 3 (Saukett 10-T) pools, which were the only ones available at the time these experiments were undertaken. Further study will indicate whether these differences are related to concentration of virus in the respective pools, or to qualitative differences among strains with respect to their sensitivity to formaldehyde.

2. *Emulsified Vaccines Inoculated Intramuscularly.*—In planning the experiments at the Polk State School, as an extension of the early studies at the D. T. Watson Home, it seemed that the first question that needed an answer was whether or not antigenic activity could be demonstrated when formaldehyde-treated fluids of all three immunologic types are incorporated together and emulsified with mineral oil. If it were possible to show that such preparations induced antibody response to all three types, an attempt would be made in the next phase to answer the question as to the relative efficiency of virus emulsified with mineral oil, as compared with similar or larger doses administered without mineral oil and inoculated via different routes, i. e., intradermally, subcutaneously, and intramuscularly.

In the first study carried out at the Polk State School (experiment P-1) a group of 16 subjects were inocu-

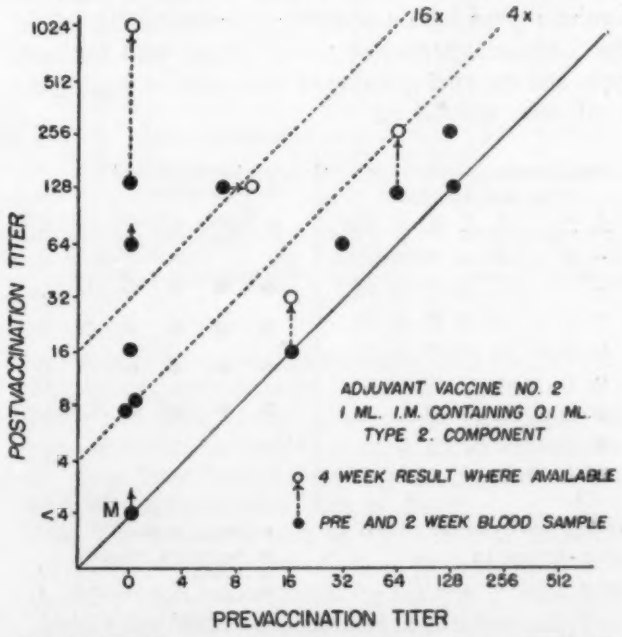


Fig. 9.—Antibody response to type 2 poliomyelitis virus in human subjects who had been inoculated with vaccine containing the three immunologic types of poliomyelitis virus. The vaccine had been treated with formaldehyde (experiment P-1). The titer is expressed in terms of the dilution of serum that was added to the virus before inoculation, and is given as the 50% end point.

lated with adjuvant vaccine no. 2, the components of which were as follows: for type 1, Mahoney pool 7, 11-T treated with formaldehyde for 7 days; for type 2, MEF-1 pool 15-K treated with formaldehyde for 10

days; and for type 3, Saukett pool 23-K treated with formaldehyde for 7 days.

Each tissue culture fluid was emulsified separately with an equal quantity of oil and was pretested for sterility before the three types were blended by mixing 4 ml. of each together with 8 ml. of mineral oil to disperse

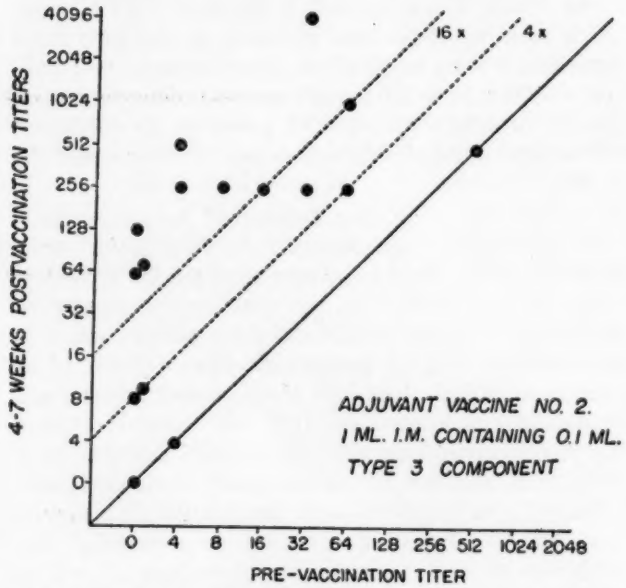


Fig. 10.—Antibody response to type 3 poliomyelitis virus in human subjects who had been inoculated with vaccine containing all three immunologic types of poliomyelitis virus after the vaccine was treated with formaldehyde (experiment P-1).

the rather thick emulsion. A dose of 1 ml. of this mixture was given intramuscularly; it contained 0.1 ml. of the formaldehyde-treated tissue culture fluid for each type, and the total quantity of tissue culture fluid in the 1 ml. dose was 0.3 ml.

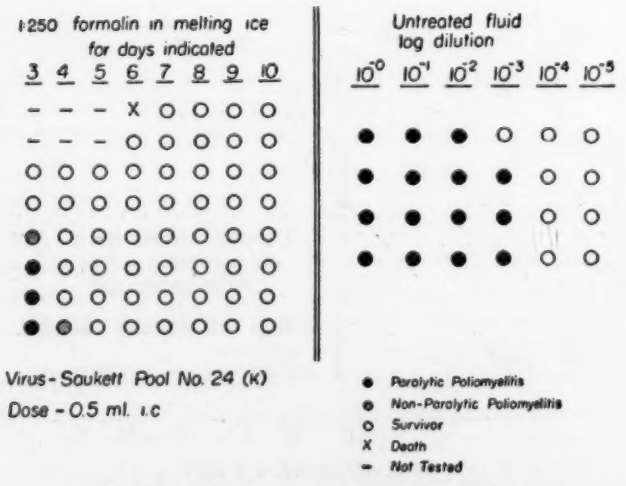


Fig. 11.—Results of infectivity tests for cynomolgus monkeys of Saukett (type 3) tissue culture fluid used for human inoculation (experiment F-22).

Titration data for type 1 antibody before and after vaccination are available in 15 of the subjects, for type 2 antibody in 12, and for type 3 antibody in all 16. Individuals for whom data are incomplete are those for whom the serologic tests need to be repeated because no end points were reached either in the pre- or postvaccination sample. The omissions, therefore, are of individuals with extremely high levels of antibody even before vaccination.

Before presenting the immunologic data for this experiment, it should be noted that the interval after vaccination is too short to reveal the full antigenic effect that can be anticipated in subjects inoculated with virus emulsified in mineral oil. The data are presented nevertheless because it has been amply demonstrated in studies with emulsified poliomyelitis vaccines in monkeys and with emulsified influenza virus vaccines in man [36] that the effects observed early tend to persist. Further justification for presenting the information derived so soon after vaccination with the emulsified material is provided by the degree of persistence of the antibody response elicited with the aqueous vaccine given intradermally in experiment W-2.

Antibody Response to the Type 1 Component of Emulsified Vaccine: The degree of antibody response to the type 1 component of adjuvant vaccine no. 2 is shown in figure 7. Here, as in a previous chart constructed in the same manner, each symbol represents one individual, and the position of each in relation to the horizontal and vertical coordinates indicates the level of antibody before and after vaccination. Symbols situated on the solid diagonal line indicate that no change in titer occurred in the interval between the taking of the pre- and postvaccination serum samples, and the perpendicular distance from the diagonal indicates the degree of change between the two. The titers in figure 7 are of the level of antibody before and at two or four weeks after vaccination; information is not yet available for the four week blood samples in all subjects, nor for later samples that have been collected.

It would appear from these results that the type 1 component of this particular vaccine was effective in inducing a rise in antibody titer. These observations were made in persons who, even though they have no history of ever having had paralytic poliomyelitis, had some antibody for type 1 virus before inoculation. Whether or not their previous antigenic experience may have been a factor in demonstrating the presence of antigenically active material in the vaccine is not as yet known.

TABLE 9.—*Comparison of Antibody Titers in Human Serum by Mouse and Tissue Culture Tests*

Exper. P-1 Subject No.	Dilution of Serum Protecting 50% of Mice *		Dilution of Serum Protecting 50% of Cultures †	
	Before Vaccination	2 Weeks After	Before Vaccination	2 Weeks After
P-25	24	417	0 ‡	128
P-87	0	128	0	> 64
P-66	0	118	0	8
P-79	0	107	0	16
P-83	0	32	0	0
P-95	0	22	0	8

* 32 LD_{50} of MEF-1 (type 2) virus used in mouse test.
† 100 $TCID_{50}$ of MEF-1 (type 2) virus used in tissue culture test.
‡ 0 = < 4.

36. Salk, J. E.; Bailey, M. L., and Laurent, A. M.: The Use of Adjuvants in Studies on Influenza Immunization: II. Increased Antibody Formation in Human Subjects Inoculated with Influenza Virus Vaccine in a Water-in-Oil Emulsion, Am. J. Hyg. 55: 439, 1952.

As was noted above, the fluid containing the type 1 virus employed in this experiment was treated with formaldehyde for seven days. Data on infectivity for cynomolgus monkeys of the Mahoney pool 7, 11(T), used in this experiment are shown in figure 8. The symbols are the same as those employed in earlier charts. It is clear that, of the monkeys that survived the observation period, there was no evidence of paralytic or nonparalytic poliomyelitis in those inoculated with fluid treated with formaldehyde for either six or seven days. The infectious activity of the fluid prior to treatment with formaldehyde is also shown in figure 8.

Antibody Response to Type 2 Component of Emulsified Vaccine: The available immunologic data for the type 2 component of adjuvant vaccine no. 2 in the same subjects are summarized in figure 9. In this figure the solid symbols indicate the pre- and two week postvaccination serum antibody titers, and where available the four week results are shown as open circles. These observations confirm the findings presented earlier (experiments W-2, 5, 7) indicating the antigenic activity of the type 2 virus after treatment with formaldehyde, this time when emulsified with mineral oil. Later blood samples are available and are at present being tested. Data on infectivity for monkeys of the fluid used in this experiment were presented in figure 5.

Table 9 shows the results of tests for type 2 antibody made in mice and in tissue culture. It is evident again (as was shown in figure 4 for experiment W-2) that the numerical value for antibody is measurably higher in the mouse test, particularly in the postvaccination serum samples. Antibody before vaccination was revealed in but one subject (P-25) in whom antibody was demonstrated in the prevaccination sample by the mouse test but not by the tissue culture test. In another subject (P-83) the tissue culture test indicated no antibody either before or after vaccination while the test in the mouse indicated a rise in titer from $< 1{:}4$ to $1{:}32$.

Merely as a matter of interest, a sample of Red Cross gamma globulin (lot no. 116) was tested along with the pre- and postvaccination serum samples shown in table 9; the titer was 691 in the mouse test and 116 in the tissue culture test. This is from the same lot of gamma globulin studied by Bodian [37] and reported by him to possess a titer of antibody for the type 2 virus similar to that shown here.

Antibody Response to Type 3 Component of Emulsified Vaccine: A summary of antibody responses to the type 3 component of adjuvant vaccine no. 2 before and four or seven weeks after vaccination appears in figure 10. The indications are that the third immunologic variety of poliomyelitis virus is antigenic when incorporated in a vaccine containing all three immunologic types. Infectivity data for the cynomolgus monkey of the formalinized preparation employed are shown in figure 11. From these data, it appears that the material employed for human inoculation was devoid of infectious activity for the number of cynomolgus monkeys used in the safety test, in which 0.5 ml. was introduced intracerebrally. All animals were studied histologically, including those that survived the 30 day period of observation.

COMMENT

Antibody Levels Resulting from Vaccination and Natural Infection.—In order to obtain some idea of the relationship of level of antibody induced by vaccination to that resulting from natural infection, antibody titers for all three immunologic types were studied in recently paralyzed patients; this was also done in a group of persons with no prior history of paralytic poliomyelitis. The recently paralyzed group are the patients at the D. T. Watson Home, and it will be recalled that these are, for the most part, young persons. The group of subjects without a past history of paralytic poliomyelitis include the nurses and other staff members at the home and some of the children who have other crippling diseases; to these have been added individuals at the Polk State School for whom quantitative antibody data before vaccination were available.

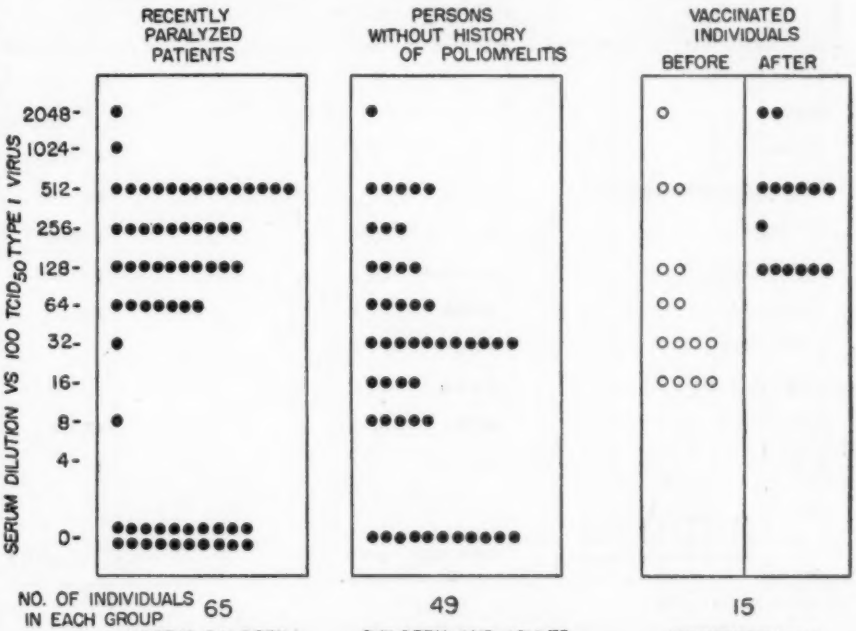


Fig. 12.—Comparison of antibody titer for the type 1 poliomyelitis virus in the serums of recently paralyzed patients, persons who had no history of poliomyelitis, and persons inoculated with poliomyelitis vaccine (experiment P-1).

It is of interest to note in figure 12 that, in recently paralyzed persons, most of whom were children, a high proportion possess antibody for the type 1 virus; and it appears that when antibody is present it is usually found in high concentration. In the group of persons without a prior history of poliomyelitis, some had no demonstrable antibody while others had antibody that was readily measurable; a point of particular interest is that, in general, the level of antibody is lower than in those who were recently paralyzed. The most reasonable explanation for this difference is that a shorter interval of time had elapsed between infection and testing in the group of recently paralyzed patients, most of whom

were children, as compared with the group who had not been paralyzed, and therefore, in whom the time of infection could not be dated.

It is interesting to observe that the 15 subjects in experiment P-1 have essentially the same distribution of antibody as the group of persons without prior history of poliomyelitis, from which they were drawn, except, of course, for the fact that there are not, in the vaccinated group, any who had no demonstrable antibody before vaccination. Following vaccination it appears that the distribution of antibody titers compares well with those of recently paralyzed patients.

Figure 13 contains similar data for type 3 poliomyelitis virus, and, when compared with figure 12, it is of interest to note that a much higher proportion of recently paralyzed patients have no antibody for type 3 virus. This is due to the fact that the majority had been paralyzed as a result of infection with the type 1 virus. Nevertheless, where antibody is present, it is found in high concentration. Here, again, in persons without prior history of poliomyelitis, there are some with no detectable antibody for the type 3 virus, and in those in whom this antibody is found, it is generally at a much lower level than in recently paralyzed subjects. Of the 16 individuals for whom data are available in experiment P-1, it is clear that they exhibit essentially the same distribution of prevaccination antibody levels as is found in the larger group of persons without a prior history of poliomyelitis, and that after vaccination there is a wide scatter, with a substantial number now with antibody levels comparable to that found in recently paralyzed patients.

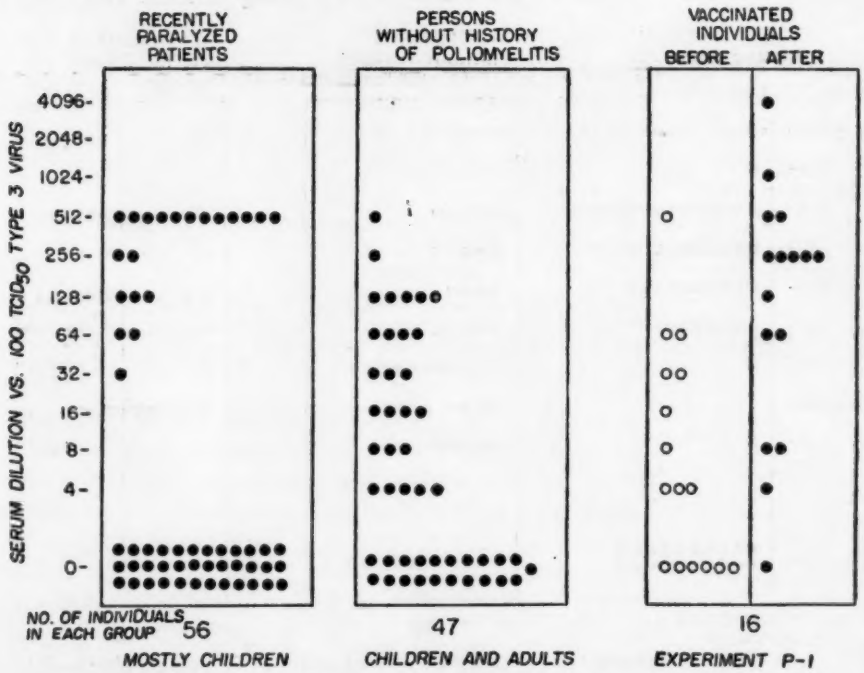


Fig. 13.—Comparison of antibody titer for type 3 poliomyelitis virus in the serums of recently paralyzed patients, persons with no history of poliomyelitis, and persons inoculated with poliomyelitis vaccine (experiment P-1).

A similar pattern for type 2 antibody is described in figure 14, and here it is of considerable interest to note the much higher proportion of recently paralyzed individuals with no antibody for the type 2 virus when compared with types 1 and 3. The majority of these patients had been paralyzed as a result of infection with the type 1 or 3 viruses, although some were paralyzed recently as a result of infection with the type 2 virus. As before, persons without prior history of poliomyelitis tend to have lower levels of antibody, and some have no detectable antibody at all. In figure 14 are combined the results of two experiments, W-5 and P-1, involving 39 persons, some of whom were vaccinated intradermally with aqueous material and others intramuscularly with virus emulsified with mineral oil. It is of interest to see here that the antibody titers of all who had no demonstrable antibody before vaccination were raised to levels comparable to that found in persons who had acquired their antibody as a result of natural infection.

The justification for combining the subjects in experiments W-5 and P-1 for the purpose of figure 14 is shown in figure 15. The two groups are not exactly the same, in that persons in experiment W-5 received two 0.1 ml. doses intradermally 6 weeks apart, and the postvaccination blood sample was tested 11 weeks after the first dose; the subjects in experiment P-1 received 0.1 ml. intramuscularly with adjuvant, and the postvaccination levels here presented are those observed two weeks after inoculation. In spite of these differences, the groups were combined to illustrate the effects that have been induced by one or another method of vaccination.

Comparison of Antibody Response to Aqueous and Emulsified Vaccines.—In the long-term plan it is expected that data will be gathered in human subjects on the relative effectiveness of vaccine administered either in the aqueous phase or after emulsification with mineral oil. Such experiments have already been performed in the sense that individuals have been inoculated; however, only a limited amount of immunologic information is now available. Although data gathered do not yet permit final conclusion, it seems worth while nevertheless to indicate the trend in tests thus far performed. The data shown in table 10 are for six subjects who were inoculated intramuscularly with the emulsified vaccine and for five subjects who received the same quantity of antigenic material intradermally in the form of an aqueous vaccine. The individuals in both groups had no antibody for type 3 virus before vaccination, but all had antibody for one or more of the other types. Although these observations are admittedly too limited for a conclusion to be drawn at this time, they suggest that incorporation of the virus with the mineral oil adjuvant may have converted what seems to be a nonantigenic preparation into one that is antigenic. This would be in keeping with the experience with influenza virus vaccines in which it was found that quantities too little to induce any demonstrable antigenic effect either in monkeys or in

the human subject, when emulsified with mineral oil were highly antigenic.[38]

Repeatability of Experiments.—The significance of the observations described in this report will not be realized until it can be demonstrated that the effects produced are repeatable. Sufficient time has not elapsed to allow the completion of all repeat experiments now in progress. Nevertheless, a limited amount of information is available, and the data at hand that bear upon this question are summarized in table 11. This table contains data showing antibody response to the type 2 virus in subjects inoculated with different vaccines prepared from two different virus pools. The data for subjects in experiments W-2 and P-1 have already appeared in previous figures and tables, but are assembled in table 11 for comparison with the results of tests in five individuals of the group included in experiment P-2 and of six subjects in experiment P-3. These are the data for all of the tests completed in subjects in experiments P-2 and P-3 at the time of writing and suggest that the experiments are repeatable, at least for the type 2 component of the vaccines employed.

Stability of Chemically Treated Poliomyelitis Vaccines.—Although there are many questions that still remain to be answered, both in the laboratory and in further clinical investigations, it is desired to present certain observations that bear on two questions that are of importance in relation to vaccines treated with chemicals for destruction of infectivity.

The first of these is the question as to whether or not treatment with sodium bisulfite to arrest the action of the excess formaldehyde may in any way effect reactivation of the virus. The data presented in figure 16 suggest that reactivation does not occur.

In this experiment, Mahoney pool 7, 11(T) was treated with formaldehyde for different periods of time at the temperature of melting ice; two different concentrations of formaldehyde were employed, and two samples were prepared. On the days indicated one sample was inoculated intracerebrally into monkeys and the second sample treated with sodium bisulfite. The neutralized mixture was then returned to a melting ice bath and 18 days later was inoculated intracerebrally into groups of five monkeys. It is perhaps unfortunate that the quantity of sodium bisulfite necessary to neutralize the more concentrated solution of formaldehyde could not be tolerated intracerebrally, and many of the animals succumbed shortly after inoculation. This can now be obviated by overnight dialysis. A more significant result is available in the sample treated with a 1:500 dilution of the formaldehyde solution which, when neutralized with sodium bisulfite, is well tolerated when given intracerebrally to monkeys. The indications are clear that the interaction with sodium bisulfite to neutralize the excess formaldehyde does not cause demonstrable reactivation of virus.

Since it is known that formaldehyde continues to act on the virus as long as the two remain in contact, the second question that had to be resolved was whether or not sodium bisulfite arrests the formaldehyde effect, and if so, does the combination of these chemicals, or some product resulting therefrom, have a deleterious effect on stability. That the simultaneous addition of sodium bisulfite and formaldehyde solution to tissue culture fluid does not impair the stability of the infectious activity of the virus is indicated by the data presented in table 12. In this experiment the solution of formaldehyde was added to fluid containing the MEF-1 virus, pool 22(K) and immediately thereafter a sufficient amount of sodium bisulfite to neutralize the excess formaldehyde, followed by a sufficient amount of sodium hydroxide to neutralize the acid resulting from this reaction. The control preparation consisted of a similar quantity of tissue culture fluid to which was added a volume of salt solution equivalent to that of the added reagents.

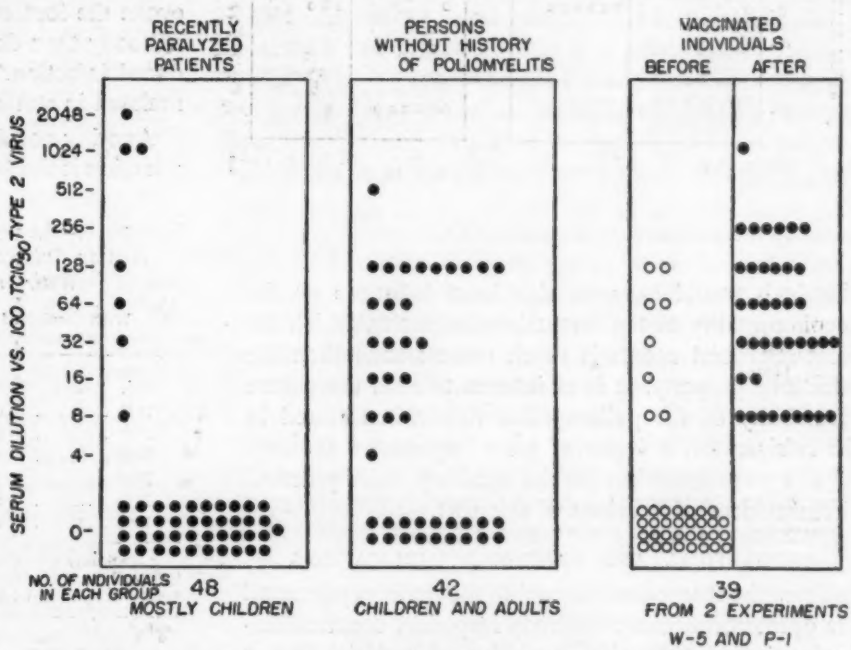


Fig. 14.—Comparison of antibody titer for type 2 poliomyelitis virus in the serums of recently paralyzed patients, persons with no history of poliomyelitis, and persons inoculated with poliomyelitis vaccine (experiments W-5 and P-1).

Each preparation was divided into two parts. One was stored in the refrigerator at a temperature of 1 to 4 C and the other was stored at room temperature, which varied between 22 and 27 C during the period of this experiment. It will be noted that when tested for intracerebral infectivity in mice, the samples kept in the refrigerator maintained infectivity at a rather constant level over the period of three months studied thus far. The slight difference between the chemically treated and the untreated control samples kept in the refrigerator may well be due to the destruction of a small amount of virus within a few moments after the addition of the formaldehyde solution and before the excess was neutralized with the sodium bisulfite. The samples

kept at room temperature both deteriorated at the same rate, thus indicating that the presence of chemicals did not affect the stability of the infectious component of the virus. It is probable that this combination of

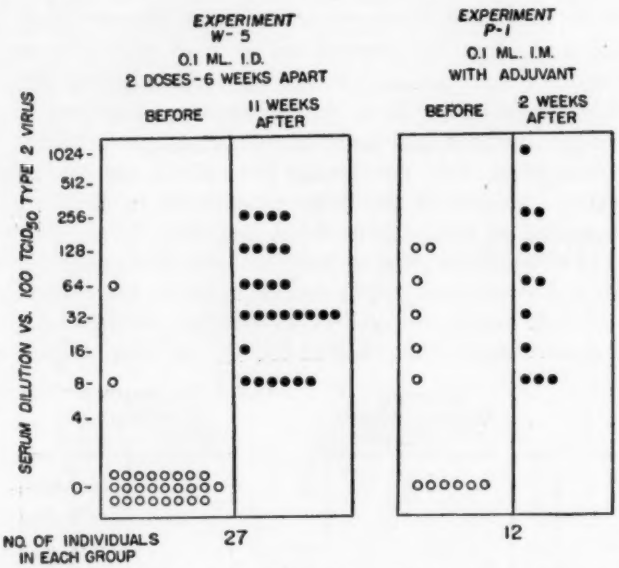


Fig. 15.—Antibody titer for type 2 poliomyelitis virus before and after vaccination in experiment W-5 and experiment P-1.

chemicals would have no significant influence on the keeping quality of the immunizing capacity, which for most microbial agents is much more stabile than the infectious property. It is of interest to note the degree of stability of the poliomyelitis virus when stored in the refrigerator, a factor of great importance not only for the preparation but for the handling under practical circumstances of vaccines of this sort.

THEORETICAL AND PRACTICAL IMPLICATIONS

From the theoretical viewpoint, the findings presented are of interest because antibody responses occurred following inoculation with quantities of material that a

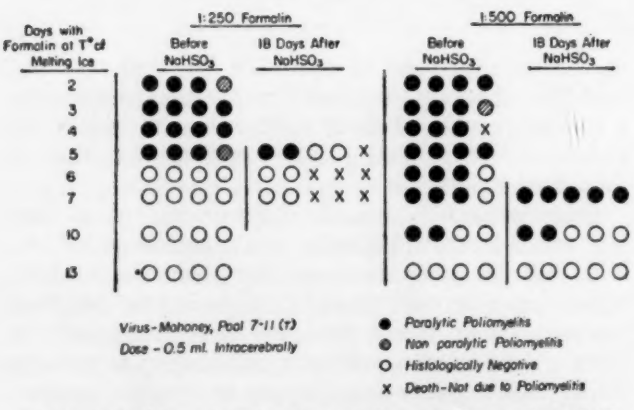


Fig. 16.—Infectivity for cynomolgus monkeys of tissue culture fluids containing the Mahoney virus treated with formaldehyde the excess of which was neutralized with sodium bisulfite.

priori might not have been expected to be effective. It may well be that the quantity of antigenic substance present in the fluids employed is considerably greater than is suggested by the results of titrations for infectious activity. It was this thesis, formulated on the basis of observations made earlier,[39] that influenced the plan for the studies here reported.

Comparative data on the antibody-inducing effect in humans of poliomyelitis virus vaccines with and without emulsification with mineral oil are meager. However, the trend in the observations here reported is in keeping with the results of studies with influenza virus vaccines, in which it has been found that a concentration of virus in sodium chloride solution, just below the threshold necessary to induce antibody formation, can be rendered antigenically effective if prepared in a water-in-oil emulsion. The efficacy of this method for inducing antibody formation with small quantities of antigen has been discussed elsewhere.[38] When a sufficient concentration of influenza virus is emulsified with mineral oil and inoculated into experimental animals, it has been possible to evoke the formation of much greater concentrations of antibody than develop as a result of experimentally induced infection.[40] Similar observations are being accumulated in studies with the poliomyelitis virus.

Another consideration to which it is desired to draw attention is the use of cultures of kidney tissue that yield,

TABLE 10.—*Serum Antibody Titers* to Type 3 Virus in Human Subjects Inoculated with Poliomyelitis Vaccine With or Without Mineral Oil Adjuvant*

With Emulsified Vaccine Intramuscularly			With Aqueous Vaccine Intradermally		
Subject No.	Before	4 Wk. After	Subject No.	Before	4 Wk. After
P-50	0	128	W-83	0	0
P-89	0	128	W-89	0	0
P-56	0	64	W-136	0	0
P-59	0	8	W-139	0	0
P-13	0	4	W-140	0	0
P-91	0	0			

* Antibody titers measured against 100 $TCID_{50}$ Saukett virus (type 3). The quantity of vaccine inoculated into each individual was that contained in 0.1 ml. of Saukett tissue culture pool no. 23 (K) treated with formaldehyde for seven days at the temperature of melting ice.

as compared with other tissues, relatively high concentration of virus into the fluids that bathe the cultured tissue. This may have been a significant factor in providing not only a rich source of virus but one relatively free of extraneous protein or other potentially antigenic material. The absence of significant amounts of tissue material, other than the virus itself, may have played a role in favoring the demonstration of the antigenic potentiality of the chemically treated virus preparations. For example, it has been found, in experiments not yet reported, that admixture of central nervous system tissue suspension with influenza virus markedly inhibits the formation of antibody specific for the influenza virus, when such a mixture is emulsified with mineral oil and inoculated into experimental animals. When influenza virus without central nervous system tissue is emulsified with mineral oil, the full potentiality of the antibody-inducing effect of the virus is evident. It would appear from this observation, which confirms findings made many years ago by Laidlaw in studies with distemper virus,[41] that the relatively small amount of virus in proportion to the total amount of extraneous tissue

mass present in brain or cord suspension might be relatively ineffective antigenically merely because of the blocking of antibody-producing "space" by the nonviral elements, and not because of the absence of antigenic capacity of the virus itself.

TABLE 11.—*Antibody-Inducing Effect of Vaccines Prepared from Two Different Pools Containing MEF-1 Strain Type 2 Virus*

MEF-1 Pool No. 15-K

Experiment W-2 †				Experiment P-1 ‡	
Before	2 Wk.	6 Wk.	8 Wk.	Before	2 Wk.
0	32 *	72	157	24	417
0	8	16	52	0	128
0	2	21	29	0	113
0	8	16	24	0	107
0	8	19	16	0	32
				0	22

MEF-1 Pool No. 26-K

Experiment P-2 §			Experiment P-3 ‖	
Before	2 Wk.	5 Wk.	Before	3 Wk.
0	348	635	4	768
0	358	...	0	389
0	358	...	0	294
0	135	...	0	168
0	45	72	0	111
			0	85

* The titers are the reciprocals of 50% neutralizing dilution vs. 32 LD_{50} type 2 virus tested in mice.

† The vaccine had been treated with formaldehyde for 13 days; 0.1 ml. of the aqueous preparation was injected intradermally. A second dose was given six weeks after the first.

‡ The vaccine had been treated with formaldehyde for 10 days; 0.1 ml. of the emulsified preparation was injected intramuscularly.

§ The vaccine had been treated with formaldehyde for 15 days; 0.1 ml. of the emulsified preparation was injected intramuscularly.

‖ The vaccine had been treated with formaldehyde for 21 days; 0.1 ml. of the emulsified preparation was injected intramuscularly.

All of the subjects included in the experiments here described possessed, prior to inoculation, antibody for one or another of the virus types. This is emphasized since it is conceivable that the immunologic response of such individuals even to virus for which they possess no detectable antibody may be different from that of persons who have no antibody for any type and are first brought into contact with the poliomyelitis virus when inoculated with vaccine. The answer to this question will soon be forthcoming. In fact, it appears from preliminary results in experiments P-3 and P-4 that antibody formation, for type 2 virus at least, occurred in six young subjects with no demonstrable antibody for any type before vaccination. Whether or not quantitative differences exist in the immunologic reactivity of persons with and without preantibody for any virus is under study. Nevertheless, it is clear that the preparations employed are antigenically active even if it is assumed that this effect has been due in part to their immunologic status before vaccination.

From the practical point of view, it is noteworthy that antibody formation has been induced in man with the very small volumes of tissue culture fluid used here. It would appear that the problem of producing a sufficient quantity of virus, even for the purpose of a noninfectious vaccine that might conceivably be used on a large scale would not be limited so long as a tissue is employed that would yield virus in a concentration not less than that present in the fluids used in these studies. In this same regard, it may be that the mineral oil may not only render effective a preparation that would not have been antigenic without emulsification but, in addition, may permit a given quantity of material to be extended further, if fluids with greater virus concentrations can be produced. It would seem from the results of the present studies with the small quantities of fluid employed that preparation of enough virus for vaccine would not be impractical even if tissue culture fluids had to be concentrated tenfold.

There are some who may object to the use of kidney tissue as the source of virus because of the unanswered question regarding organ damage by immunization with material emulsified with mineral oil. Although many theoretical arguments as well as examples by analogy may be brought forth to indicate that such effects are improbable with the material employed, it still remains for studies that are underway to indicate whether or not it will be necessary to purify the virus by chemical or physical means in order to insure that such immunologic reactions will not occur if such vaccines are used on a large scale or if more than one injection has to be given.

In one experiment in progress, a group of seven monkeys is being inoculated repeatedly with 20% kidney suspension emulsified with mineral oil. After four weekly injections of 1 ml. each, there is no gross clinical evidence of abnormality. Kidney tests and urinalyses as well as histological studies are to be performed. Tests with serum from guinea pigs inoculated with 20% suspension of monkey kidney tissue emulsified with mineral oil are also in progress. The indications are that precipitation does not occur when such serum is mixed with tissue culture fluid from which vaccine is prepared. However, precipitins in the serums are evident when a 1% suspension of monkey kidney tissue is mixed with the antikidney serum. These are but qualitative tests and merely indicate that there is present in culture fluids very little kidney protein. Quantitative experiments are in progress. It may be worth mentioning that no evidence of dermal sensitivity has been observed in any of 64 subjects given two or more inoculations of kidney culture fluid intradermally. In six subjects who received two doses of vaccine, with adjuvant, three weeks apart, no untoward reaction has been evident clinically.

TABLE 12.—*Stability at Different Temperatures of MEF-1 Virus * in Tissue Culture Fluids Containing Formaldehyde Plus Sufficient Sodium Bisulfite to Neutralize the Excess Formaldehyde†*

Time After Addition of Reagents	Neg. Log. of Infectivity Titers for Mice of Samples At Refrigerator Temperature of 1-4 C.			At Room Temperature of 22-27 C.		
	Formaldehyde and $NaHSO_3$	Control	Log. Diff.	Formaldehyde and $NaHSO_3$	Control	Log. Diff.
1 hr.	...	...	.....	3.0	3.7	−0.7
1 day	3.4	3.2	+0.2	3.5	3.4	+0.1
2	...	...	.....	4.0	3.9	+0.1
3	3.2	3.6	−0.4	3.0	2.8	+0.2
5	...	...	.....	2.2	3.0	−0.8
7	3.0	3.6	−0.6	1.8	1.9	−0.1
14	3.1	3.5	−0.4	1.4	2.1	−0.7
21	3.5	3.8	−0.3	2.0	1.7	+0.3
3 mo.	3.5	4.0	−0.5	0	0.4	−0.4

* MEF-1 Pool No. 22 (K).

† 1:250 dilution of "formalin" (37% solution of formaldehyde, U.S.P.).

Every effort has been made to reduce the likelihood that virus particles capable of multiplication might be present in the preparations employed for human inoculation so that any danger of inducing disease would be reduced or eliminated. Another equally important purpose was to learn whether or not virus multiplication is essential for antibody formation and, particularly, for its persistence. If virus multiplication is not essential then it should be possible to gain information on the limits of antigenic mass required to induce a persistent effect both with or without mineral oil adjuvant.

From the data presented, it appears that the preparations inoculated into human subjects were devoid of infectious activity for the monkey; this has been corroborated in rigorous tests performed in tissue culture. In spite of these facts there are some who may feel that satisfactory proof of total destruction of capacity to multiply will not be had until the virus is further concentrated for the purpose of increasing the chance of detecting the one particle that may not yet have undergone change to the noninfectious state. It would seem that conditions for destruction of infectivity could be selected at which the likelihood is so small that infectious activity is present as to make it possible to suggest that it is probably absent, not only for practical purposes but theoretically as well. In the studies presented an effort was made to use such preparations only.

The question is present in the minds of many in regard to the degree of persistence of the antibody formed after infection with fully infectious virus as compared with that resulting from the injection of noninfectious material. It would seem to be unwise at this time to maintain the view that a noninfectious preparation cannot be made to reproduce, in some degree at least, the immunologic effects that occur following natural or experimentally induced infection. The indications from the total experience with mineral oil emulsified vaccines support the thesis that with adequate attention to the quantitative factors involved, it is possible, with noninfectious material to approximate, and perhaps to exceed, the level of antibody induced by infection. This is the objective of the present approach and the data here presented are intended merely to convey the earliest indications that this may be possible.

A very significant new development in the field of poliomyelitis virus cultivation is that of Cox and his associates,[42] who have reported the propagation of a type 2 strain in the developing chick embryo. It is to be hoped that it may some day be possible to cultivate viruses of the other two types in this way and that concentrations can be achieved that are comparable to those obtained by methods employing cultures of primate tissues.

SUMMARY AND CONCLUSIONS

Preliminary results of studies in human subjects inoculated with different experimental poliomyelitis vaccines are here reported. For preparation of these vaccines virus of each of the three immunologic types was produced in cultures of monkey testicular tissue or monkey kidney tissue. Before human subjects were inoculated, the virus was rendered noninfectious for the monkey by treatment with formaldehyde.

In one series of experiments it appears that antibody for all three immunologic types was induced by the inoculation of small quantities of such vaccines incorporated in a water-in-oil emulsion. In another series of experiments, antibody formation was induced by the intradermal inoculation of aqueous vaccines containing the type 2 virus. Information at hand indicates that the antibody so induced has persisted without signs of decline for the longest interval studied thus far, i. e., four and a half months after the start of the experiment.

Levels of antibody induced by vaccination are compared with levels that develop after natural infection. The data thus far available suggest that it should be possible with a noninfectious preparation to approximate the immunologic effect induced by the disease process itself.

Although the results obtained in these studies can be regarded as encouraging, they should not be interpreted to indicate that a practical vaccine is now at hand. However, it does appear that at least one course of further investigation is clear. It will now be necessary to establish precisely the limits within which the effects here described can be reproduced with certainty.

Because of the great importance of safety factors in studies of this kind, it must be remembered that considerable time is required for the preparation and study of each new batch of experimental vaccine before human inoculations can be considered. It is this consideration, above all else, that imposes a limitation in the speed with which this work can be extended. Within these intractable limits every effort is being made to acquire the necessary information that will permit the logical progression of these studies into larger numbers of individuals in specially selected groups.

Laboratory Medicine.—In most branches of medicine the individual physician is still the indispensable man and his functions cannot as yet be mechanized. In the field of laboratory medicine, however, there is an increasing tendency to relegate to a secondary position the role of the individual and to exalt the apparatus, the test, and the report. This accentuation of the inanimate in medicine is a trend to be deplored and strongly resisted. Like all habits it reduces the resourcefulness of the individual, and it is especially pernicious in that it further weakens those who are already irresolute.

There are physicians in all branches of medicine who at times are unable to reach a prompt diagnosis on clinical grounds alone. Before the era of the ascendancy of laboratory medicine such men would often call on a more experienced colleague for consultation. In most cases such tutorial help would elucidate the clinical features present and would leave the physician much richer in knowledge not only for the benefit of the patient at hand but also for the future. With the rise of laboratory medicine the role of the clinical consultant has been to a large extent erased, and physicians have tended more and more to rely on the laboratory to make the diagnosis for them. Unfortunately, those physicians whose clinical judgment is the poorest are also the ones who are most inclined to accept laboratory reports without question as being final and impeccable. Such a blind dependence on laboratory diagnosis does very little to develop clinical judgment and skill.—Marcus Rayner Caro, M.D., Diagnostic Pitfalls of Dermal Pathology, *A. M. A. Archives of Dermatology and Syphilology*, January, 1953.

FOUR FATAL CASES OF BULBAR POLIOMYELITIS IN ONE FAMILY

Max J. Fox, M.D.
and
John Chamberlain, M.D., Milwaukee

Many reports have appeared over the years concerning multiple cases of poliomyelitis in individual families, but we have found none that compared with the severity of the involvement of this Milwaukee family in the fall of 1952. The family consisted of mother, father, and eight children, but the eldest son was on the West Coast with the Marine Corps and the eldest daughter was living away from home at the time of the catastrophe. Thus, only six of the children were exposed to the infection; four of them were stricken with the bulbar form of poliomyelitis, and all four died of it.

The family lived in a small well-kept home on the outskirts of Milwaukee in a semirural area. They grew all their own vegetables and obtained their water from a private well in their back yard. Both of these sites were ruled out as sources of infection by the city health department. The family also had two healthy geese and a collie dog. A month before the onset of the children's illnesses a parakeet was found in the yard, and advertising for the owner without success, the family decided to keep the bird as a pet. When found, the bird's stools were noted to be green. Because of the severity and course of the bulbar-encephalitic involvement in the children and their close contact with the parakeet, it was sent to the Federal Security Agency, Public Health Service, in Montgomery, Ala., but no virus was isolated. The home was small and conditions necessarily crowded, so B. L. and L. L. slept in the same bed. M. L. slept in the same room with her two sisters, but in a separate bed. P. L. slept with a 12-year-old brother who was unaffected. No definite contacts or source of infection could be determined.

REPORT OF CASES

CASE 1.—P. L., aged 17, a star football player for a local high school, was admitted to St. Mary's Hospital, Milwaukee, on Sept. 14, 1952, at 7:15 a. m. with severe headache and pain and weakness of his right arm and shoulder. The pain in his shoulder had begun on Sept. 10th, when he injured it in football practice. Despite the pain he had continued to play football on the next four days. Slight headache had begun in the afternoon of Sept. 13, accompanied by an earache. Next morning he was awakened with a severe pounding headache and his mother noted some change in his voice. When he entered the hospital he was having difficulty in breathing and had an uncontrollable tremor of the head.

Examination revealed a well-developed white boy in some distress, but alert and cooperative. Blood pressure was 140/72 mm. Hg, pulse rate 120 per minute, respiration 24 per minute, and temperature 101.6 F. A gross tremor of head and tongue was noted. In the right arm all muscle groups, including those of the shoulder girdle, were weaker than on the left side. A diagnosis of poliomyelitis was made, and he was transferred to South View Hospital, Milwaukee, at noon, Sept. 14. A lateral nystagmus was present. The tympanic membranes looked dull and somewhat opaque, though not bulging. The pharynx was moderately injected. The right nostril was completely blocked, and a seropurulent discharge was coming from the mucous membrane of both nostrils. His neck showed advanced rigidity. Temperature was 101.6 F, pulse rate 120, and respiration 28. The spinal fluid was clear under slightly increased pressure and contained 87 cells per cubic millimeter, 90% polymorphonuclears and 10% lymphocytes; glucose 66 mg. per 100 cc.; chloride 716 mg.; and total protein 60 mg. per 100 ml.

Courses of penicillin, acetylsalicylic acid, and neostigmine (prostigmin®) bromide were begun, but the patient continued to complain of headache and pain in his right arm and shoulder. His appetite was poor, but he had no difficulty in swallowing on the day of his admission. His temperature remained at about 101 F, and profuse sweating continued throughout the day. Jerking movements of his right arm became pronounced, and the tremor of his head continued. Soon after midnight on Sept. 15 he began to vomit frequently, the vomitus being liquid and of coffee-ground color. Around 2 a. m. he began to have difficulty swallowing and mechanical aspiration of the pharynx was begun. He slept only for short periods and began to show considerable apprehension. At 8 a. m. his rectal temperature was 100.6 F, pulse rate 110, and respiration 34 per minute. Marked weakness of his left arm as well as the right was now present, and muscle twitching of both upper extremities continued. One unit of plasma followed by 500 ml. of 5% glucose in an isotonic sodium chloride solution was given intravenously. His apprehension increased through the day, his rectal temperature reaching 103.4 F, pulse rate 124, and respiration 50 per minute. His cough reflex had almost entirely ceased, and profuse amounts of mucus were continually being aspirated from his throat. Nasal oxygen was instituted. His skin was flushed, and sweating was almost continuous throughout the day. Around 5 p. m. he became moderately cyanotic and his skin felt cold and clammy, but he continued to be fairly well oriented though markedly apprehensive. Coramine® (25% solution of nikethamide) was given, and the oxygen was increased to 12 liters per minute, with little objective improvement. He was placed in a respirator at 6:30 p. m., but continued to decline and died at 6:50 p. m.

Clinical Course of Four Fatal Cases of Bulbar Poliomyelitis

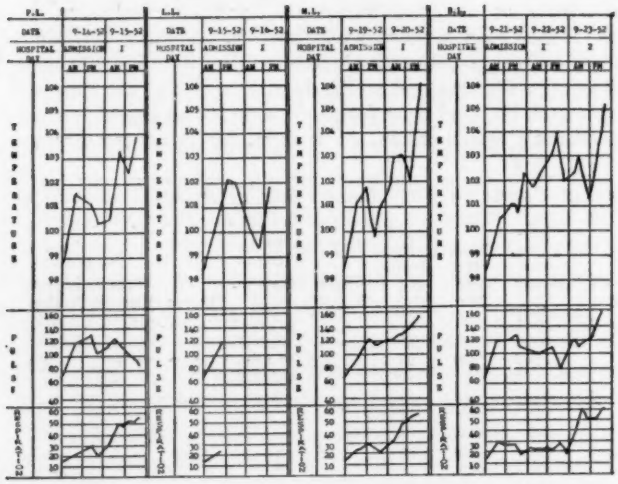
Patient	Temperature Range, F	Pulse Rate per Min.	Respiration Rate per Min.	Neck Rigidity	Paralysis	Coma	Sore Throat	Vomiting
P. L.	100.2 to 103.8	90 to 130	20 to 50	.....	Marked weakness in upper extremity	None	+	++
L. L.	99.4 to 102	100 to 140	20 to 30	.....	None	None	+	+
M. L.	99.8 to 106	100 to 154	20 to 60	.....	None	None	++	++++
B. L.	100.6 to 105	84 to 100	20 to 60	None	None	None	++++	++++

CASE 2.—L. L., a girl aged 4, was in good health until the morning of her admission on Sept. 15, when she complained of headache and pain in the neck. She entered South View Hospital at 2 p. m. with a temperature of 102 F, pulse rate of

From the Department of Internal Medicine, Marquette University School of Medicine, and the South View Isolation Hospital.

130, and respiration 28 per minute. She did not seem to be acutely ill and could swallow without difficulty. Her skin felt warm and dry, and she did not seem to be dehydrated. The right eardrum was markedly injected and slightly bulging. The tonsils were large and the throat mildly injected. Her neck was doubtfully rigid. In the heart a systolic murmur was audible over the pulmonary area. Spinal fluid was clear under normal pressure, containing 924 cells per cubic millimeter, 99% polymorphonuclears and 1% lymphocytes; 56 mg. glucose per 100 cc.; 704 mg. chloride; and 54 mg. total protein per 100 ml. Peripheral blood studies showed 4,360,000 red blood cells per cubic millimeter and 12,750 white blood cells per cubic millimeter: 65% polymorphonuclears, 31% lymphocytes, and 4% monocytes. Sedimentation rate was 30 mm. in one hour.

She was treated by general supportive measures with acetylsalicylic acid for her headache. The evening of the day of her admission she began to have difficulty in swallowing and vomited slightly. That night she rested well but continued to complain of a severe headache. Next day, Sept. 16, she ate well, had only slight difficulty in swallowing, and had no more vomiting. She ate a good supper that evening and went to sleep soon afterwards in apparently good condition. She was observed frequently and seemed to be sleeping and breathing



Temperature, pulse rate, and respiration rate changes in four patients with bulbar poliomyelitis during their hospital stays.

normally. Ten minutes after the last check, the resident on duty found that her pulse and respiration had ceased and she did not respond to artificial respiration. She was pronounced dead at 8:20 p. m.

CASE 3.—M. L., a girl aged 8, was admitted to the hospital on Sept. 19 with sore throat, general weakness, headache, stiff neck, and a weak voice. Two days before she had complained of sore throat and had been slightly feverish. On the day before her admission she vomited several times and complained of increasing headache. She had had her tonsils removed early in 1952 after recurrent bouts of tonsillitis. On admission she was a well-developed, well-nourished girl, in no acute distress. Temperature was 101.2 F, pulse rate 100, and respiration 22 per minute. Spinal fluid was clear under normal pressure; containing 88 cells per cubic millimeter, 99% polymorphonuclears and 1% lymphocytes; 70 mg. glucose per 100 cc.; 704 mg. chloride; and 37 mg. total protein per 100 ml. Microscopic examination of the urine showed many white blood cells. Sedimentation rate was 41 mm. in one hour.

The child's condition remained essentially the same until evening. She was cooperative and could swallow without difficulty, though she ate very little dinner and refused her supper. In the early evening she became apprehensive and had a large projectile emesis, but she soon fell asleep and spent a good night. When she awoke next morning, she took a little water and soon afterwards vomited clear fluid. She began to have difficulty swallowing, and a marked nasal "twang" appeared in her speech. She was given 300 ml. of plasma followed by 500 ml. of 5% glucose in an isotonic sodium chloride solution intravenously. She continued to vomit frequently, some of the vomitus returning through her nose. By 8 a. m. she could no longer swallow her own saliva, so oral suction was begun. Her temperature had risen to 103 F, pulse rate to 124, and respiration to 32 per minute. Her apprehension increased progressively through the day. At 10 a. m. she began to vomit large amounts of blood-tinged fluid and mucus collected in her throat. Penicillin therapy was begun, and nasal oxygen was administered at 6 liters per minute. At 11 a. m. she began to sweat profusely and her skin became cold and clammy, but by 12:30 p. m. the blood-tinged mucus subsided considerably and her skin again felt warm. By 3 p. m. her respiration had become shallow at 52 per minute, with a pulse rate of 140. She vomited a coffee-ground-colored fluid several times and became moderately cyanotic. The oxygen was stepped up to 10 liters per minute, and her color improved, though her temperature had risen to 104.4 F by 5 p. m. and she began to complain of double vision. At 6 p. m., despite acetylsalicylic acid and ice-packs, her temperature rose to 106.2 F, her respiration became shallower at 50 per minute, and her pulse was thready at 154 per minute. She continued to respond coherently to questions until 6:15 p. m. when she died, having failed to respond to coramine® or artificial respiration.

CASE 4.—B. L., a girl aged 13, was admitted to the hospital at noon on Sept. 21. The evening before she had begun to complain of a severe headache with vertigo, nausea, and a mild fever. These complaints had increased in severity with the addition of scotomas at the time of her admission. When first examined she felt very sick but had not vomited. She did not complain of any difficulty in swallowing and had no stiffness of her neck or back. She was markedly apprehensive, because she recognized her symptoms as similar to those of her brother and sisters. On admission she was well-developed, well-nourished, and in no acute distress. Temperature was 100.6 F, pulse rate 120, and respirations 28 per minute. Blood pressure was 128/70 mm. Hg. Her throat was markedly injected, especially in the right tonsillar area, where the uvula was adherent. The spinal fluid was clear under normal pressure and contained 28 cells per cubic millimeter, 50% polymorphonuclears and 50% lymphocytes; 71 mg. glucose per 100 cc.; 723 mg. chloride; and 38 mg. total protein per 100 ml. Peripheral blood studies on her second day in the hospital showed 5,380,000 red blood cells per cubic millimeter; hemoglobin 15 gm. per 100 ml.; 20,000 white blood cells per cubic millimeter; and 21% lymphocytes. Sedimentation rate was 50 mm. in one hour; hematocrit, 50%.

At the time of her admission (1 p. m.), her temperature was 100.6 F, pulse rate 120, and respiration 28 per minute. She had no difficulty in swallowing but began to vomit regularly about 3 p. m. She spent a fairly good first night, though her temperature reached 103 F. She was given 1 unit of plasma, followed by 1,000 ml. of 5% glucose in isotonic sodium chloride intravenously, and elixir of diphenhydramine (benadryl®) hydrochloride, minims every four hours, was given to allay her apprehension. Her temperature rose to 104 F at 8 p. m. Her blood pressure was 130/60 mm. Hg, pulse 120, and respiration 28 per minute. She continued to be restless, but her general condition seemed to be satisfactory, and her vomiting was less frequent. Cortisone, 250 mg., was given at 10 p. m. At 3 a. m. on the 23rd she complained of a severe throbbing headache and her skin looked pale and mottled. Coramine,® 4 ml., was given intravenously with 500 ml. of whole blood, and nasal oxygen was started with considerable improvement. Her temperature was 102.4 F, pulse 140, respiration 50 per minute, and blood pressure 130/106 mm. Hg. At 7 a. m. she began to bring up large amounts of blood-tinged mucus, which she could spit out with little difficulty. Her condition remained

fairly stable during the day; she remained fully oriented and her temperature remained at about 102 F, pulse rate 120, respiration 50 per minute, and blood pressure 120/80 mm. Hg. One unit of plasma, followed by 1,000 ml. of 5% glucose in isotonic sodium chloride with amino acids, was given intravenously. She continued to vomit coffee-ground material at intervals, but the blood-tinged mucus decreased in amount. At 4:30 p. m. she became more apprehensive and the mucus secretions increased. Her blood pressure fell to 72/50 mm. Hg, and her skin again became mottled. The nasal oxygen was increased to 12 liters per minute, and coramine® was given, but she failed to respond. Her temperature rose to 105 F, pulse rate 160, and respiration 60 per minute; she died at 8 p. m.

NECROPSY FINDINGS

The gross appearance of the central nervous system in each of the four cases was essentially the same, namely, severe congestion and swelling of the cerebral convolutions. In each case the cortex was salmon-pink. Petechial hemorrhages were noted particularly in the left dentate nucleus, in the floor of the fourth ventricle, and in the pons, medulla, and anterior horns of the spinal cord. There were no significant differences in the gross visceral changes in the four cases, but the following minor exceptions were noted microscopically. The patient in case 4 had pulmonary hemorrhages, bronchopneumonia, moderate interstitial myocarditis, and petechial hemorrhages into the adrenals, whereas the one in case 1 had a minimal interstitial myocarditis with surface myocardial hemorrhages and a minute basophil adenoma of the pituitary.

Microscopic examination of the central nervous system in the cases also revealed much the same findings. In all cases there was a very severe inflammatory reaction involving the spinal cord, medulla, pons, dentate nucleus of the cerebellum, and leptomeninges of the spinal cord and brain stem. Mononuclear reaction was also present in the leptomeninges of the cerebral hemispheres. The changes, however, were somewhat severer in case 1, in which petechial hemorrhages were more numerous and larger and the horn areas of the spinal cord and portions of the medulla showed actual liquefaction necrosis in minute microscopic areas. The distribution of the changes in the medulla was about the same in each case, but perhaps there was a somewhat greater involvement of the medial reticular substance of the medulla in case 4.*

COMMENT

Multiple cases of poliomyelitis in one family are no rarity. In the great epidemic of 1916, out of 8,634 families attacked in New York City, 4.2% were reported as having more than one case.[1] Swartout and Frank reported 9.29% of multiple cases in the 1943 epidemic in Los Angeles, the increased incidence probably being due to the fuller diagnosis of abortive cases.[2] However, the finding of four cases of fatal bulbar poliomyelitis in one family is fortunately unique. The reports that involve multiple cases of bulbar poliomyelitis are found for the most part in articles describing the incidence of this form of the disease following tonsillectomy brought to the fore by Francis, Krill, Toomey, and Mack in 1941 and 1942; they describe one family in which five healthy children were subjected to tonsillectomy on the same day; poliomyelitis developed in all five, and three died.[3] In the family reported on in this present paper, no surgical procedure had been carried out for over two months before the onset of their illness. (P. L. had had a herniorrhaphy on July 2, 1952.)

From the studies of Aycock and Eaton and others it would appear that the four members of this family contracted their disease from a single primary source rather than from one another, as the onset of their illnesses fell within seven days of one another.[4] Even though the particular strain of the virus has not yet been isolated, it is evidently a particularly virulent one, since all the monkeys inoculated with it either died or were paralyzed. The possibility that these children were unusually susceptible to the virus remains hypothetical.

SUMMARY

Four fatal cases of bulbar poliomyelitis in children in one family are reported, only one of which showed any signs of spinal involvement. All four children died within eight days. Virology studies verified the clinical diagnosis.

324 E. Wisconsin Ave. (Dr. Fox).

* Dr. Joseph F. Kuzma, Director of Laboratories, Milwaukee County Institutions, made the necropsy reports.

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Hospital Morale.—Good hospital and clinic service demands loyalty among the staff members to each other and to the institution. Loyalty and a willingness to serve on the part of the nursing force and the pupil nurses and a loyal spirit among the nonprofessional personnel can be easily built up. Such loyalty will develop a cooperative family spirit in the institution which will, in turn, furnish an excellent service to the patient.

Poor judgment is often displayed in choosing the nonprofessional personnel of our hospitals and clinics, especially those who come in intimate contact with the public—the receptionist, those in the admitting office, the clinic and dispensary clerks, the telephone operators, those who run the elevators, the ambulance crew, the nurses' aides and the ward maids. It is wise not to allow people to meet the public until they have had extensive training in handling the public tactfully.

If our hospitals can be robbed of their cold institutional atmosphere by little touches of human kindness; if the patients are treated more as individuals and less as cases, and if management and the nursing force will cooperate with the staff in planning for the patient's welfare, I am satisfied there will be much less criticism on the part of the general public.

Maeterlinck said, "If the bee colony is to survive through the long winter the spirit in the hive must be good." This spirit among the workers in our hospitals must be excellent if we are to maintain good hospital morale.—D. Guthrie, M.D., Humanities in Hospital Practice, *Postgraduate Medicine*, January, 1953.

CLINICAL NOTES

INDEPENDENT CARCINOMAS OF COLON OCCURRING TWENTY-ONE YEARS APART

REPORT OF A CASE

Claude F. Dixon, M.D.
Clyde A. Pitchford Jr., M.D.
and
Samuel P. McCarran, M.D., Rochester, Minn.

It has been stated that the microscopic appearance of a recurrent neoplasm will determine whether it represents progression of the original neoplasm or a completely new growth.[1] Normal mucosal glands are observed abruptly adjacent to a recurrent growth, whereas in the metachronous growth the transition from normal to malignant cells at the margin of the growth is gradual. Also, there is a difference in the clinical behavior of recurrent and of metachronous growths.[1] It has been found that the former appear at an average of three years after operation and that the final postoperative survival time is a year and a half. The average interval between operations for primary and for metachronous growths is four years, and the postoperative survival time is about five and a half years. Close follow-up care of all of these patients is necessary in order that carcinomatous transformation can be detected early. Regardless of whether a recurrent neoplasm represents a metachronous growth or the original neoplasm, the patient probably should undergo a further operative procedure, especially if distant metastasis is not demonstrable. Gratifying results of such a plan, that is, reasonably long postoperative survivals, have been described.[2]

REPORT OF A CASE

When first seen, May 25, 1931, the patient was a student, 26 years of age, whose mother had died of carcinoma of the bowel. His complaint was of intermittent cramping pain in the left upper and left lower quadrants of the abdomen that began an hour after eating, lasted for several minutes to an hour or more, and was accompanied by gurgling and the passage of flatus. During the 10 months since onset of these symptoms, he had noticed increasing constipation and finally had resorted to the use of laxatives. Occasionally, streaks of blood and mucus were present on the feces. At times, his bowels did not move for two or three days. He had felt feverish at times and also had lost 23 lb. (10.4 kg.) in 10 months.

Positive findings on examination were body temperature, 101 F; tenderness in the left upper quadrant of the abdomen, where palpation suggested the presence of a mass; leukocytes 22,000 per cubic millimeter of blood; and hemoglobin, 70% (11.2 gm. per 100 cc.). Roentgenologic study of the colon following barium enema revealed an obstructive lesion at the splenic flexure.

On June 1, 1931, while he was under spinal and ethylene anesthesia, the patient's abdomen was explored through a left upper rectus incision. A carcinoma of the splenic flexure without apparent metastasis was found. Blind cecostomy was performed. The postoperative course was uneventful except for occasional episodes of abdominal cramps. On July 13, 1931, with the patient again under the same anesthesia, a large, perforating carcinoma of the splenic flexure was resected, and the ends of the colon were brought out through the abdominal wall as in obstructive resection. The tumor was the size of an adult's fist and was difficult to remove. The pathologists reported the presence of an annular adenocarcinoma, grade 2, without demonstrable involvement of lymph nodes. On Nov. 2, 1931, the colonic stoma was closed. Because the patient was young, the prognosis was thought to be poor. On June 7, 1935, the patient had maintained a good weight and had maintained his strength. His bowels moved once a day. There was almost constant seepage from the cecal stoma, which was closed surgically.

On July 13, 1951, the man returned for observation. He was then a salesman and was 46 years old. His symptoms and investigation of his gastrointestinal tract indicated the presence of duodenal ulcer; consequently, a regimen for ulcer was prescribed; however, he complained of loss of energy and occasional cramps in the left upper quadrant of the abdomen. He stated that on one occasion in 1950 he had passed blood with his stool. Proctoscopic examination and roentgenologic investigation of his colon gave normal results.

On Jan. 8, 1952, the patient returned. He stated that the cramping left upper abdominal pain was increasing in severity and that it was relieved after passing flatus. He had one or two bowel movements daily that did not contain visible blood or mucus. In general, he did not feel quite well. Roentgenologic examination by his home physician had disclosed the presence of what seemed to be a stricture at the site of the former colonic anastomosis. By April 1, 1952, the cramping pain was occurring about four times a day, and, sometimes, it lasted for four hours. The man thought that he could feel gas and fecal material rumbling through the left upper quadrant of his abdomen. Roentgenograms of his colon were made after barium enema. The site of the anastomosis was unobstructed and was functioning; however, because of the symptoms of obstruction, an exploratory operation was carried out on April 7. A transverse incision in the left upper part of the abdomen revealed a large, ulcerating carcinoma at the site of the previous anastomosis of the colon. The lesion was removed by obstructive resection, using a three-bladed clamp. The pathologist reported the tumor to be an adenocarcinoma, grade 4, at the old operative site. It was annular, ulcerating, and obstructing and involved the pericolonic fat and several regional lymph nodes by direct extension. The microscopic picture was that of a new, independent, primary growth of the colon. When this report was being written, the patient was convalescing from closure of the colonic stoma. This had been effected about six weeks after the obstructive resection.

COMMENT

It is interesting that the prognosis at the time the first carcinoma was removed was poor. The patient's youth was a factor in the poor prognosis, and also it has been observed that the five year survival rate for patients who have obstructive carcinoma of the left part of the colon is just half that for patients who have nonobstructive carcinomas at the same site.[3]

From the Division of Surgery, Mayo Clinic (Dr. Dixon) and the Mayo Foundation (Drs. Pitchford and McCarran).

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TOXOPLASMOSIS FOUND BY RECOVERY OF TOXOPLASMA GONDII FROM EXCISED AXILLARY GLAND

REPORT OF A CASE

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and
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Toxoplasmosis as a disease of man was first observed by Jankû in 1923.[1] Since that time this protozoal disease has been found with increasing frequency, especially among infants. The causative organism was first established in 1939.[2] The disease in infants is usually manifested as a form of encephalitis with such features as hydrocephalus or microcephaly, chorioretinitis, microthalmos, and intracerebral calcification. Cases of active toxoplasmosis among adults, confirmed by isolation of the causative organism, have been relatively few in number, approximately a dozen, and often have proved fatal. These cases have usually been manifested by a prolonged remittent fever with such features as pneumonitis, encephalitis, myocarditis, and maculopapular rash, and have borne little resemblance to the disease in infants.

Toxoplasmosis of the newborn is apparently contracted from the mother, who acquires the infection during pregnancy and who, while usually free of symptoms pointing toward the disease, nevertheless, gives serologic evidence of the infection. Moreover, immunologic studies of human serums from various localities show that the percentage of positive reactors increases with age, reaching a level of 25 to 65% among adults who usually give no history suggesting infection with Toxoplasma organisms.[3] Thus it appears that inapparent or unrecognized instances of this infection must be quite common among persons who have lived to adulthood.

Siim, in 1951,[4] reported seven cases, six children and one adult, who by serologic evidence appeared to have acquired toxoplasmosis. The principal clinical finding in these cases was generalized lymphadenopathy. The enlarged firm, discrete, painless nodes found in the necks, axillas, and groins were, in three instances, the sole findings and were discovered only on examination. Attempts to demonstrate Toxoplasma micro-organisms from one of the excised glands by microscopic examination and by animal transmission were unsuccessful.

The case of toxoplasmosis here reported is of interest because it is the first instance, to our knowledge, in which toxoplasmosis has been diagnosed by recovery of the parasite from a localized superficial adenitis.* It occurred in an adult, not suspected of having this disease until after he had recovered. The diagnosis was established by the recovery of Toxoplasma gondii from an excised axillary gland removed on the 53rd day after onset of illness and by the demonstration of a high titer of antibodies in the patient's serum.

REPORT OF CASE

A 44-year-old Negro male grocery truck driver was admitted to Gallinger Municipal Hospital, Washington, D. C., on Sept. 24, 1951.† He had been well until Sept. 10, when weakness, generalized aching, and loss of appetite developed. On Sept. 19 he experienced high fever, chills and sweats, nausea, and a generalized headache, symptoms that persisted to admission. He was stated to have lost 30 lb. (13.6 kg.) in weight since onset of his present illness.

The patient appeared rational but acutely ill; the temperature was 104 F, pulse 120, respirations 30, and blood pressure 120/75 mm. Hg. The skin was hot and dehydrated, with no rash. All joints were freely movable, and the neck was supple. There were no enlarged glands; the fundi were normal; nose and throat were normal; and heart sounds were of good quality. There were moist inspiratory rales at the right lung base posteriorly. The liver was palpable 1 fingerbreadth down. The spleen was not palpable. Neurological findings were normal.

Laboratory tests showed hemoglobin 12 gm. per 100 ml.; white blood cells 10,900 per cubic millimeter, with 67% neutrophils, 21% lymphocytes, and 12% monocytes; and sedimentation rate 39 mm. per hour, corrected (Wintrobe). The urine had a specific gravity of 1.020, a pH of 5.5, and contained no albumin. There were traces of sugar and acetone, which were not present on subsequent examination. The sediment contained approximately 5 erythrocytes, 5 leukocytes, and 2 coarsely granular casts per high power field. Cold agglutination titers of 1:1,024 on Sept. 27, 1:512 on Oct. 3, 1:128 on Oct. 10, and 1:4 on Nov. 1, 1951, were obtained. Eight cultures of blood, one of sputum, one of stool, and one of marrow yielded no pathogenic organisms. Agglutination tests for typhoid, paratyphoid, Brucella abortus, and Proteus X19 gave negative results on admission and three weeks later. Smear and culture of bone marrow for tubercle bacilli were negative. Malaria parasites were sought in the blood on two occasions without success. The heterophil antibody titer was 1:7. No sickling of erythrocytes was demonstrable. Chest roentgenogram revealed slight diffuse haziness of both lung fields. Sinus roentgenograms showed relative clouding of the right frontal and maxillary sinuses. Flat film of the abdomen and intravenous pyelogram were within normal limits.

During the patient's first two days in the hospital the temperature reached 104 F and 105 F. The fever persisted thereafter for 30 days with spiking elevations from 98 to 102.8 F. Primary atypical pneumonia was the initial diagnosis, and a course of 300,000 units of procaine penicillin per day for 10 days was given intramuscularly without apparent effect. Aureomycin was then administered orally, 500 mg. every six hours for three days without effect. Antibiotic medication was then discontinued. The fever continued to reach 101 and 102 F daily. The rales at the right base disappeared around Oct. 5. On the 45th day of illness a single soft, tender lymph node, the size of a pecan, was noted in the right axilla. This led to the consideration of cat scratch disease as a diagnostic possibility. The nonsuppurating lymph node was removed on the 53rd day after onset of illness, for microscopic examination, culture, and inoculation into animals. The same day 0.1 ml. of cat scratch disease antigen of established potency was injected

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From the Laboratory of Infectious Diseases, National Microbiological Institute, National Institutes of Health, Public Health Service (Dr. Armstrong), and George Washington University Medical School (Dr. MacMurray).

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* Since this report was submitted a case of acquired toxoplasmosis, in a 17-year-old girl, confirmed by the demonstration of Toxoplasma in mice inoculated with a superficial gland removed at biopsy, has appeared.

† Dr. Hugh H. Hussey, Chief of Georgetown University Hospital Medical Service, Gallinger Municipal Hospital, permitted the report of this case.

intradermally; the result after 48 hours was equivocal. The complement fixation test employing the patient's serum and lygranum® antigen (lymphogranuloma venereum antigen from yolk sac of embryo of chick) was negative. The patient's course in the hospital was one of slow improvement, and he was discharged, 53 days from onset, apparently in good health.

A fraction of freshly removed axillary gland was delivered at the National Institutes of Health on Nov. 2, 1951. The gland was macerated without abrasive and suspended in buffered sodium chloride, pH 7.6. A rhesus monkey was immediately inoculated intracutaneously with .1 ml. of the gland suspension in each of several areas. The animal remained well, and neither lesions at any of the inoculation sites nor any other symptoms developed. One guinea pig was likewise inoculated with .1 ml. of the gland suspension intraperitoneally and another subcutaneously. Both remained apparently well and afebrile except that the intraperitoneally inoculated animal showed a temperature of 104 F on the 16th day, but the temperature was normal the following day and remained so. The animals were discharged on Jan. 3, 1952.

Six white mice (NIH strain) were also inoculated, each with .03 ml. of the gland suspension intracerebrally and .2 ml. intraperitoneally. The mice were observed daily without noteworthy developments until Jan. 25, 1952, when two mice were noted to be rather quiet and to remain apart from their cage mates. On Jan. 31, one of the ill mice was noted to be blinking his eyes frequently, to be tremulous and unsteady on his feet, and at times to sit up, rub his nose, and jerk his head. The mouse was etherized and the brain emulsified in sodium chloride, and 12 fresh mice were inoculated intracerebrally with .03 ml. and intraperitoneally with 0.1 ml. of the brain suspension, which proved to be sterile to culture. Four days later six of the mice were ill and the fur was rough. They sat quietly and on being disturbed were tremulous and unsteady. When picked up by the tail they tended to become spastic. The remaining six mice were ill the next day, and all mice either died or were sacrificed. Successive transfers were easily maintained. The agent proved not to be filtrable and did not withstand freezing or storage in 50% glycerin. Inoculated mice tended to have difficulty breathing, and at autopsy the lungs were often pneumonic and markedly congested having a uniform red to nearly black appearance. The spleen was usually somewhat enlarged, and the chest and peritoneal cavities often contained several milliliters of thick sticky exudate. Giemsa-stained impression smears from the surfaces of the brain, lungs, and peritoneal organs revealed many protozoa both in enlarged cells and free, which resembled T. gondii in all particulars. They were pathogenic for both guinea pigs and rabbits. On Feb. 4, 1952, the second of the originally inoculated two ill mice was etherized and the brain transferred to six fresh mice as was done in case of the mouse first mentioned. All six mice showed symptoms on the fourth day, transfers were continued, and Toxoplasma micro-organisms readily demonstrated. The remaining four originally inoculated mice were discarded through error and could not be further studied.

Results of the Sabin-Feldman Dye Test for Immunity Against Toxoplasmosis Using Human and Cat Serums

Patient	Date Serum Was Collected	Stage of Illness	Result	Remarks
S. G.	11/ 2/51	Convalescing	+1:32,000	Repeated twice
	5/ 7/52	Recovered	+1:250	Repeated twice
W. W.	1/16/51	Convalescing	+1:1024	Repeated + 1:512
	3/28/51	Recovered	+1:1024	.....
P. S.	1/16/51	Convalescing	+1:64	.....
	3/28/51	Recovered	+1:64	.....
D. I.	3/28/51	Convalescing	+1:64	.....
Cat (F. A.)	4/ 7/52	Well	+1:128	.....
15 serums (10 patients)	Various dates	Ill patients	+Undiluted	.....
25 serums (14 patients)	Various dates	Ill patients	—	.....
Cat	4/24/51	Well	—	.....

Serologic studies of the patient's serums, employing the Sabin-Feldman dye test,[5] were performed by Dr. Leon Jacobs of the Laboratory of Tropical Diseases, National Microbiological Institute. Serum drawn 53 days from onset of illness revealed a titer of 1:32,000, while serum collected 187 days later when similarly tested gave a titer of 1:250. Complement fixation studies by the Subsection on Immunology, Laboratory of Tropical Diseases, with the Nov. 2, 1951, serum were anticomplementary and with the May 7, 1952, serum positive in a 1:5 dilution. Toxoplasma micro-organisms in sections of a fraction of the gland could not be demonstrated. Dr. Jacobs examined 44 serums from 28 suspected cat scratch fever patients and from 2 cats associated with cases that were submitted for examination by Dr. Worth B. Daniels and one of us (F. G. M.). The results are shown in the table.

COMMENT

Toxoplasma bacteria have been recovered from many wild and experimental animals as well as birds; however, spontaneous infection with stock mice is apparently rare.[6] In this laboratory thousands of stock mice have been employed often with prolonged periods of observation without spontaneous infection with Toxoplasma micro-organisms having been recognized.

Thus the existence of the organisms in at least two of six injected mice points toward the gland suspension as the source of the infection. The interval of 137 days from injection to onset of symptoms in mice is not opposed to this view, since we have encountered mice experimentally inoculated that developed recognizable symptoms only after a lapse of time up to 171 days. Moreover, the existence of a positive Sabin-Feldman dye test in a titer of 1:32,000, employing the patient's serum collected on the day the gland was excised, confirms the existence of a recent active Toxoplasma infection, and the patient's symptoms are compatible with this diagnosis.[7] The finding of a second cat scratch disease case (W. W. in the table) whose serum gave a positive dye test titer in a dilution of 1:1024 further suggests the desirability of considering toxoplasmosis as a diagnostic possibility in cases of unexplained acute adenitis.

SUMMARY

A nonfatal infection with Toxoplasma gondii in an adult man is described in which the initial clinical diagnosis of atypical pneumonia was made, with cat scratch disease being later considered. The diagnosis was established by isolation of the causative organism from a soft, tender, nonsuppurating enlarged axillary gland removed 53 days from onset of illness. Other superficial glands were not noticeably enlarged. The patient's serum withdrawn when the gland was removed 53 days from onset gave a titer of 1:32,000 with the Sabin-Feldman dye test, and serum drawn eight months from onset gave a titer of 1:250. Toxoplasma micro-organisms were not recognized in sections of the human gland.

1150 Connecticut Ave., N.W. (Dr. MacMurray).

5. Sabin, A. B., and Feldman, H. A.: Dyes as Microchemical Indicators of a New Immunity Phenomenon Affecting a Protozoon Parasite (Toxoplasma), Science **108**: 660-663, 1948.

6. Sabin, A. B.: Toxoplasmosis: A Recently Recognized Disease of Human Beings, in Advances in Pediatrics, edited by A. G. De Sanctis, New York, Interscience Publishers, Inc., 1942, vol 1, pp. 1-56.

7. Sabin,[6] Pinkerton, H., and Weinman, D.: Toxoplasma Infection in Man, Arch. Path. **30**: 374-392 (July) 1940. Kass, E. H., and others: Toxoplasmosis in the Human Adult, A. M. A. Arch. Int. Med. **89**: 759-782 (May) 1952.

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT OF THE COUNCIL

A calculated risk is taken whenever one prescribes or administers a potent therapeutic agent. The degree of risk varies considerably, depending on the particular drug involved and the condition of the patient. A useful drug should not be condemned or avoided completely simply because it is occasionally capable of causing serious reactions.

Certain harmful effects from new drugs often are relatively infrequent and may not be brought to light until after such agents have been on the market for a considerable period of time. Responsible pharmaceutical firms recognize their obligation to the medical profession in matters of this kind and endeavor to inform physicians regarding any serious side-effects which occasionally may result from use of their products.

Penethamate hydriodide (neo-penil®), a product of Smith, Kline and French Laboratories, has not been submitted to the Council nor considered for acceptance and inclusion in New and Nonofficial Remedies. Nevertheless, the firm voluntarily furnished the information on which the following report is based. Smith, Kline and French Laboratories is deserving of commendation for its prompt cooperation in this matter.

R. T. STORMONT, M.D., *Secretary.*

SEVERE ANAPHYLACTOID AND FATAL REACTIONS TO PENETHAMATE HYDRIODIDE (NEO-PENIL®)

Penethamate hydriodide (neo-penil®), essentially a penicillin preparation, is rather unique in that it is an iodide salt and has a special affinity for lung tissue. The latter characteristic would suggest that the drug may have some special virtue in the treatment of acute and chronic pulmonary infections caused by penicillin-sensitive organisms.

A few deaths from an anaphylactic-like shock reaction have occurred after the injection of various preparations of penicillin. In the past six months, 14 severe anaphylactoid reactions, including 3 that resulted in death, have followed the administration of penethamate hydriodide. These cases represent the total number reported to Smith, Kline and French Laboratories and discovered by the firm in a rapidly conducted survey following the first report of a death.

In general, the signs of an anaphylactoid reaction to this hydriodide of a penicillin G ester are similar to those reported following administration of sodium, potassium, or procaine penicillin G; however, muscular twitching and convulsive seizures were much more frequent in this small series, occurring in 11 of the 14 patients. In 9 of these patients this reaction occurred almost immediately or within five minutes after injection. In one patient, convulsive seizures began 10 hours after administration of the drug.

In a general mailing to physicians the firm states:

"'Neo-Penil' is a new compound, differing pharmacologically from other forms of penicillin. And, as is often the case after a new compound has been in general clinical use for some time, it now develops that the toxicity of 'Neo-Penil' presents somewhat more of a problem than was recognized when it was first introduced. Further experience has indicated that its toxicity (and possibly its allergenicity) is greater than that of procaine penicillin. Furthermore, 'Neo-Penil', like procaine penicillin, may be highly toxic when injected into a vein.

With the rapidly increasing use of 'Neo-Penil', we are receiving some reports of serious reactions, and three fatalities have occurred during the course of 'Neo-Penil' therapy. The reactions appear to be similar to those described by Mayer et al. (*J. A. M. A.* **151**:351 [Jan. 31] 1953) and others, who have reported anaphylactic-like shock and convulsive reactions due to penicillin or procaine hypersensitivity; but it is possible that inadvertent injection into a vein may have been a contributing factor (in one case, at least, blood was observed at the site of injection after withdrawal of the needle)."

Physicians should ascertain from their patients before administering any form of penicillin whether any allergic manifestations followed previous use of a preparation of this drug. If there is any doubt, a scratch or intradermal test should be performed, utilizing the penicillin preparation to be administered as the allergen.

A negative skin test does not necessarily mean that a systemic reaction to the drug will not occur. Nevertheless, it is a wise precautionary measure which may serve to obviate a number of serious reactions.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, *Secretary.*

Penicillin for Oral or Sublingual Administration (See New and Nonofficial Remedies 1952, p. 122).

Chas. Pfizer & Company, Inc., Brooklyn.

Tablets Potassium Penicillin G (Buffered): 50,000, 100,000, 250,000 and 500,000 units. Buffered with calcium carbonate.

Folic Acid-U.S.P. (See New and Nonofficial Remedies 1952, p. 456).

Premo Pharmaceutical Laboratories, Inc., South Hackensack, N. J.

Tablets Folic Acid: 5 mg.

Methylthiouracil (See New and Nonofficial Remedies 1952, p. 408).

Schwarz Laboratories, Inc., New York.

Tablets Methiacil: 50 mg.

COUNCIL ON PHYSICAL MEDICINE AND REHABILITATION

APPARATUS ACCEPTED

The following additional product has been accepted as conforming to the rules of the Council on Physical Medicine and Rehabilitation of the American Medical Association for inclusion in Apparatus Accepted. A copy of the rules on which the Council bases its action will be sent on application.

RALPH E. DE FOREST, M.D., *Secretary.*

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Mijit Atomizer

The Mijit Atomizer is in the form of a small translucent bottle with an unusual double cap. The top of the cap protects the lower part and it can be removed by unscrewing. The lower part is the atomizer mechanism, which contains a slender tube that dips into the solution. The solution is contained in a translucent bottle or vial made of an elastic substance that can be compressed between the fingers.

The capacity of the vial is 25 cc., but when filled it contains 10 cc. of solution and 15 cc. of air. When pressed quickly and repeatedly it acts in a double capacity as the pressure bulb and the reservoir of an atomizer system. The atomizer alone weighs 8 gm.

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SPECIAL MEETING OF THE HOUSE OF DELEGATES

A special meeting of the House of Delegates of the American Medical Association was held in Washington on Saturday, March 14, to consider a plan for the reorganization of the Federal Security Agency. It was the fourth such special session in the history of the 106-year-old organization but was historic because the House was addressed by the President of the United States. This was the first time that a President of the United States had appeared personally before the House of Delegates, although President Coolidge addressed the opening meeting of the American Medical Association when it held its annual convention in Washington in 1927.

In spite of the fact that the meeting in Washington was a special session and that it was impossible to make plans for it as far in advance as is usually possible, almost all of the delegates were present. Following a call to order by Speaker James R. Reuling, the invocation was said by the Rev. Edward L. R. Elson, minister of the National Presbyterian Church of Washington, which is attended by President Eisenhower. Within a few minutes the presidential party, including Mrs. Oveta Culp Hobby, arrived.

President Eisenhower with an air of warm informality welcomed the delegates and officers of the American Medical Association to Washington and promptly turned to the role of medicine in public affairs. He asserted that he believed the decisions that would be reached by the House, particularly as they are related to the functions of government, would represent what the members thought would be best for the United States. Then he mentioned philosophical bonds that he had in common with the physicians of this country, among them a dislike for compulsion and a dislike for socialism. He referred to the fact that this country is spending billions to prevent socialism and to preserve our traditional system of freedom of enterprise. In no uncertain terms he claimed that this is the doctrine of the administration, of the Republican party, and of the Republican leaders in Congress. He assured his audience that these persons live by such a philosophy and intend to practice it.

Referring to the importance of the profession to society, the President stressed the meeting of the medical needs of the population. Affirming his faith in the belief that Americans want to do the right thing, he expressed confidence that the doctors will provide the needed medical services but that they can do it better with the cooperation and friendship of the administration rather than by its direction or under that of any big "poobah" in this field.

After a brief introduction to the subject before the House of Delegates, Dr. Louis H. Bauer presented Sen. Robert A. Taft, who also was enthusiastically welcomed by the House. Mr. Taft paid tribute to the fight of the medical profession in this country against the extension of socialism and said that unfortunately too few persons realize the scope of the profession's struggle to preserve freedom for the people and for those who believe in "our free economic system." He urged support for Reorganization Plan No. 1 of 1953, a plan that proposes the creation of a department of health, education, and welfare. It was presented to the Senate and House of Representatives on March 12, 1953. In effect the plan would reorganize the Federal Security Agency. In the organization section of this issue of THE JOURNAL is more information on the plan; in the next issue will be the proceedings of this special meeting of the House of Delegates. Included will be Mr. Taft's comments and his reasons for supporting the reorganization plan. He believes that the director of a department of health, education, and welfare should sit with the cabinet so that this director can be continuously exposed to the benefits and philosophy of others in high government offices and so that the activities of the department can be coordinated with other government activities and at the same time permit, in fact require, closer liaison with the President. These and other actions would prevent, Mr. Taft believes, such a department from becoming too independent and so acting.

After an explanation by Dr. Louis H. Bauer of the actions of the Board of Trustees to keep itself informed until the House could meet, Dr. Walter Judd, congressman from Minnesota, addressed the House and he too urged support for the reorganization plan. As one who is experienced in governmental and political problems, Dr. Judd offered some interesting information on what happens when policy is determined in federal government circles. Dr. Elmer L. Henderson, a past president of the American Medical Association, was presented to the House by Dr. John Cline, immediate past president, and he too urged support of the plan. Then the following report by the Board of Trustees was read by the chairman, Dr. Dwight H. Murray, and was adopted:

"The House of Delegates of the American Medical Association has for nearly 80 years been on record as favoring an independent Department of Health in the federal government. The reason for this stand has been that the House has felt that health and medicine should

be given a status commensurate with their dignity and importance in the lives of the American people, and that they should be completely divorced from any political considerations.

"The Board of Trustees, after a careful study of the policy of the American Medical Association with respect to the administration of health activities in the Executive Branch of the government and after studying the Reorganization Plan for elevation of the Federal Security Agency to cabinet status submitted by President Eisenhower to the Congress, finds that Reorganization Plan No. 1 of 1953 provides for a special assistant to the Secretary for Health and Medical Affairs. This provision is a step in the right direction which should result in centralized coordination under a leader in the medical field of the health activities of the proposed department. Health, therefore, is given a special position. The proposed plan, properly administered, will permit more effective coordination and administration of the health activities of the new Department without interference or control by other branches.

"Previous attempts to raise the Federal Security Agency from an independent agency to the level of an Executive department have been opposed by the Association because the plan did not meet these aims.

"Inasmuch as federal health benefits and programs are established by the Congress, an administration bent on achieving the nationalization of medicine cannot reach that goal except with the support of Congress. Therefore, an organizational plan through which federal health activities are administered, although important, is not nearly so vital an issue as the policies adopted by the Congress of the United States.

"The Board of Trustees recommends that the House of Delegates reaffirm its stand in favor of an independent Department of Health but that it support the Reorganization Plan No. 1 of 1953 as being a step in the right direction; that the American Medical Association cooperate in making the plan successful and that it watch its development with great care and interest.

"It should be understood, however, that the Association reserves the right to make recommendations for amendment of the then existing law and to continue to press for the establishment of an independent Department of Health, if the present plan does not, after a sufficient length of time for development, result in proper advancement in and protection of health and medical science and in their freedom from political control."

This meeting of the House is of historic significance. It was attended by the President of the United States and such renowned men as Senator Taft and Congressman Judd. In addition, however, it provided another opportunity for American medicine to express itself and for others to observe the democratic way in which physicians move in their professional and organizational circles as they study the ways in which they can meet their responsibilities.

TRACHEOTOMY IN CRUSHING INJURIES OF THE CHEST

The indications for tracheotomy, which are reasonably well established in acute laryngotracheobronchitis and bulbar poliomyelitis, have been expanded during the past few years to include such diverse conditions as cerebrovascular accidents, fracture of the skull with prolonged coma, tetanus, barbiturate poisoning, recurring postoperative atelectasis, laryngeal and bronchial edema due to flash burns, and the postoperative care of critically ill patients who have been subjected to esophagectomy, neurosurgical procedures, or other extensive surgical operations. More recently, Carter and Giuseffi [1] have focused attention on the role of tracheotomy in the treatment of crushing injuries of the chest.

As a result of the mechanized tenor of contemporary life, injuries resulting from severe compression of the chest are steadily increasing. "Crushed chest," "flail chest," and "stove-in chest" are terms used interchangeably to describe a form of nonpenetrating injury characterized by multiple rib fractures that cause paradoxical movement of the affected segment of the thorax. This type of injury is commonly associated with trauma to the head, extremities, and viscera of the abdomen and thorax and may include such complications as hemothorax, pneumothorax, and "wet lung."

In persons with crushing injuries of the chest there are characteristic respiratory findings. Breathing is short and rapid and is usually accompanied by considerable pain and apprehension. In addition, cyanosis, tachycardia, and rapid respiration generally occur. The act of coughing enhances pain and increases the paradoxical movement of the affected segment of the thorax. Although the tracheobronchial tree is dry initially, except when parenchymal injury to the bronchi or lungs exists, it may later be filled with secretions to produce a "wet lung." When this takes place, a vicious circle is established: Cyanosis and rapid respiration assist in establishing the "wet lung" syndrome, which, in turn, produces increased paradoxical movement of the injured segment of the chest wall. Since the presence of pain makes coughing ineffectual, the tracheobronchial tree is cleared imperfectly and secretions stagnate within the alveoli and bronchioles to further impair mechanical ventilation of the affected lung.

A large number of therapeutic measures have been employed through the years, with no single procedure gaining widespread acceptance, ranging from simple adhesive strapping to complicated forms of operative skeletal fixation. Carter and Giuseffi report that they have satisfactorily treated 11 patients with crushing injuries of the thorax, utilizing tracheotomy as a primary form of therapy. They found that tracheotomy reduces the paradoxical movements of the injured chest segment; alleviates pain, since it decreases the movement of the fractured ribs; and provides a ready method for aspirating tracheobronchial secretions. Moreover, they believe tracheotomy promotes two physiological effects:

1. Carter, B. N., and Giuseffi, J.: The Use of Tracheotomy in the Treatment of Crushing Injuries of the Chest, Surg., Gynec. & Obst. 96: 55 (Jan.) 1953.

a reduction in the amount of dead space in the respiratory tree and a decrease in resistance to breathing, both on inspiration and on expiration.

In general, treatment of crushing injuries of the chest should be individualized. According to these authors, if the chest injury is of either minor or moderate degree, intercostal nerve block should be used and the patient carefully observed. If, subsequently, the act of coughing fails to raise secretions properly and if respiratory embarrassment occurs as the result of the accumulation of tracheobronchial exudate, tracheotomy is performed without hesitation. Finally, in the event trauma to the chest is severe, tracheotomy is performed immediately. The tracheotomy tube is removed when the general condition of the patient has improved, when the breathing difficulties have been resolved, and when fixation of the rib fractures has been sufficiently established to prevent the reappearance of paradoxical respiration and pain.

INTRAOSSEOUS INFUSIONS

When significant quantities of fluid must be given to a patient parenterally, the intravenous route is usually preferred. If, however, as a result of obesity, edema, extensive burns, circulatory collapse, or other factors the superficial veins are not accessible to puncture, other routes must be used. One of the most useful of these, and one that is frequently overlooked, is the intraosseous route. This is in fact merely another intravenous route, since the vascular spaces of bone marrow communicate directly with numerous large veins emerging from the bone; thus material injected into the marrow appears immediately in the general circulation.[1] By way of the sternal, ilial, or tibial marrow, large volumes of blood, plasma, glucose, and electrolyte solutions can be given rapidly and continuous infusions of heparin, antibiotics, anesthetic solutions, and other drugs can be administered.[2] For the introduction of viscous solutions such as blood, positive pressure may be necessary, but solutions of lesser consistency can be introduced at a satisfactory rate by gravity alone.

The technique of intraosseous infusion has certain advantages over other techniques that may be used when superficial veins become inaccessible. In an emergency, sternal, iliac, or tibial puncture can be performed more rapidly with less equipment and less light than can surgical exposure and cannulization of a peripheral vein or artery. Under conditions of civilian or military disaster, this feature assumes particular importance. In addition, a needle inserted in bone is more stable during continuous or repeated infusions than a needle in a peripheral vessel, and its use allows the patient greater freedom of movement. Insertion of a stilet into the needle between infusions prevents occlusion by clots. Solutions of glucose or amino acids can be given safely and rapidly by intraosseous infusion, whereas these same solutions given by hypodermoclysis may cause oliguria and circulatory collapse in patients with dehydration, salt deficiency, or incipient shock.[3] Only isotonic electrolyte solutions administered with hyaluronidase can be given rapidly enough by hypodermoclysis to be of value in an emergency. Intraosseous transfusion has the advantage over intra-arterial transfusion that it does not jeopardize the circulation of distal parts. In some cases of deep shock, however, intra-arterial transfusion may restore normal blood pressure when intravenous (or intraosseous) transfusion will not.

The potential hazards of intraosseous therapy, which in the past have sometimes discouraged its use, have been reduced to a minimum by improvements in technique and equipment.[4] The threat of secondary osteomyelitis has been largely eliminated by the use of strict asepsis and, when necessary, antibiotics. The possibility of producing embolism by forcing cortical fragments into the marrow cavity at the time of the initial puncture has been minimized by the use of a trephine-type needle,[2] which removes intact a tiny plug of cortical bone rather than driving it inward. The hazard of perforation through the entire sternum or ilium due to too sudden or forceful a thrust on a pointed needle has also been eliminated by the use of the trephine needle, which permits controlled pressure.

In infants as well as in adults intraosseous infusion has been found to be a useful alternative to peripheral intravenous therapy in emergencies or in any case in which the latter is not practical.

IMMUNOLOGICAL EFFECTS OF CORTISONE

Investigators have recently reported that administration of cortisone to rabbits inhibits the production of antibodies after primary injections of specific vaccines. Cortisone would thus presumably prevent the development of an effective convalescent immunity in many infectious diseases. These findings have been confirmed and extended by Fischel [1] and his associates of Columbia University to include the effect of cortisone on antibody production following secondary or "booster" injections of specific antigens.

The Columbia clinicians tested rabbits immunized several months previously against crystallized egg albumin. Four days before the planned administration of the "booster" dose, one-half of the rabbits were placed on a daily dose of 25 mg. of cortisone acetate. The cortisone therapy was continued for 17 days. In the untreated control rabbits there was a marked and precipitous rise in antibody titer after the "booster" injection. None of the cortisone-treated animals showed an increase in antibodies. It seems evident from these data that cortisone therapy may interfere with the use of "booster" vaccines, a phenomenon worthy of careful clinical investigation.

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1. Tocantins, L. M.: Rapid Absorption of Substances Injected into the Bone Marrow, Proc. Soc. Exper. Biol. & Med. **45**: 292 (Oct.) 1940. Reprinted in Am. J. Med. **11**: 568 (Nov.) 1951.

2. Tarrow, A. B.; Turkel, H., and Thompson, M. S.: Infusions via the Bone Marrow and Biopsy of the Bone and Bone Marrow, Anesthesiology **13**: 501 (Sept.) 1952.

3. Abbott, W. E., and others: The Danger of Administering Parenteral Fluids by Hypodermoclysis, Surgery **32**: 305 (Aug.) 1952.

4. Texter, E. C., and Kaump, D. H.: Intraosseous Infusions in Infants, J. Mich. M. Soc. **47**: 1002 (Sept.) 1948.

1. Fischel, E. E.; Vaughan, J. H., and Photopoulos, C.: Inhibition of Rapid Production of Antibody by Cortisone: Study of Secondary Response, Proc. Soc. Exper. Biol. & Med. **81**: 344 (Nov.) 1952.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

For the fourth time in history the House of Delegates of the American Medical Association was called in special session. What I have to say about it will be no news to the members of the House, but I believe the other 130,000 members should know the whole story lying behind the call. The call was issued because of the proposed elevation of the Federal Security Agency to the status of an executive department. On several occasions during the past 80 years the Association has gone on record in favor of a department of health at executive level. I believe it was not so much that the Association wanted a health representative in the cabinet as that it felt health had too long been a stepchild and that it deserved a status commensurate with its dignity and importance in the lives of the American people.

Twice during the last administration the Association went all out to defeat reorganization plans that would have raised the Federal Security Agency to an executive level. Why then was a special meeting of the House necessary? Why could not the Association's officers have gone ahead and fought this new plan? The reasons follow.

Both the previous attempts would have made health the "tail of the dog." There was no reason to believe that the plans would have done anything but provide increasing political control over medicine, and that, in fact, both attempts were primarily political plays. The well-known philosophy and the prior actions of the then Federal Security Administrator only confirmed us in such an opinion. During the election campaign, the medical profession was led to believe that, if a change came about in Washington, there would be no further talks about socializing medicine and there would be cooperation with the profession in solving health problems. Consequently, almost as soon as the election was over, requests were made by your Board of Trustees for conferences so that the whole situation could be thoroughly explored. The fullest cooperation of the Association was tendered the new administration.

Shortly after the inauguration, a delegation consisting of the President, the President-Elect, the Chairman of the Board, the Chairman of the Legislative Committee, the Secretary and General Manager, the Assistant Secretary, and the Director of the Washington office held a conference with the new Federal Security Administrator, Mrs. Oveta Culp Hobby. The conference was most helpful. Our group could not have been more cordially welcomed, and it was evident to all of us that henceforth the door to the Administrator's office was wide open at any time to us. We all felt certain that cooperation and understanding would now be the order of the day. We were sure that any recommendations we might make in the future would be courteously received and carefully considered. A liaison committee was appointed by the Board with the approval of the Administrator, to serve in any way that would be helpful. The committee consists of Drs. Elmer L. Henderson, Louis H. Bauer, Edward J. McCormick, Dwight H. Murray, and F. J. L. Blasingame, with Walter B. Martin as an alternate.

The day following the conference with the Administrator, the President, President-Elect, Chairman of the Board, and Director of the Washington office conferred with the President of the United States. Again, we were most cordially received and many matters were discussed. We all came away with the feeling that at last medicine had a "friend at court." Some of our group also conferred with members of Congress. As a result of our conferences, it became apparent that we were alone in desiring an independent department of health. The opinion within the Administration and Congress appeared to be that there were already too many independent agencies and that some should be combined rather than split up. One argument given was that the federal government made a grave error in splitting up the Department of Commerce and Labor into two departments, for, as a result, there are now two departments both dealing with business, industry, and labor, and better coordination could be had in one department.

I had stated on this page in December that we wanted an independent health department not tied in with education or with social security. It was called to my attention that both education and social security have programs that are not necessarily primarily medical but have medical phases and that such phases could not be brought under a department of health. It was also stressed that a separate department of health, under an unfriendly administration, would well engage in empire building and prove to be the dragon that would devour us. While such could happen no matter what the arrangement, it would be less apt to happen if there were not a separate department. I must confess that this argument left me at a loss for an answer.

Since it was apparent that there was no possibility of a separate department of health, and since it was also known that a reorganization bill would be introduced into Congress to change the status of the Federal Security Agency from an agency to an executive department, we were all anxious to see that the best possible status be established for health and medicine. After telephone conversations with the President and the Federal Security Administrator, conferences were arranged with the reorganizing committee and the Administrator. Dr. Blasingame and I attended the first; Drs. McCormick, Murray, Blasingame, Martin, Lull, McCarthy, Howard, and Wilson, and Mr. Stetler and I attended the second.

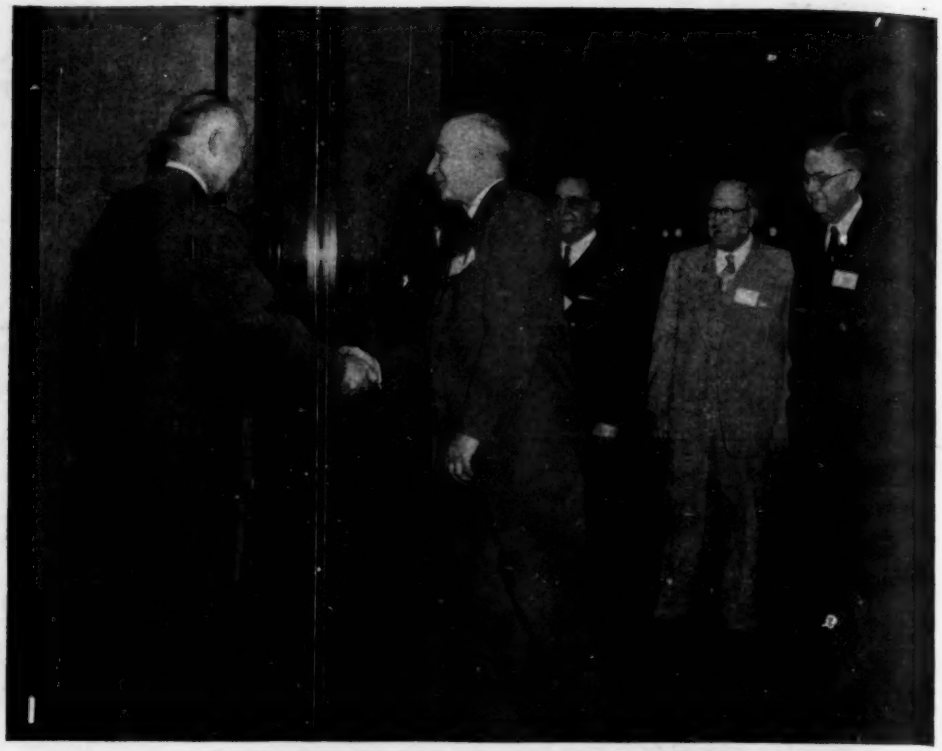
All our suggestions were received with interest and were largely adopted. As a result the reorganization plan introduced provided a new position, that of a special assistant to the Secretary. All medical activities within the new department, as well as all medical phases of any activities within education or social security, must be cleared through this special assistant to the Secretary. This will include appropriations and budgets as well as policies. The same special assistant will also be the representative of the Secretary at all interdepartmental meetings at which health will be a topic for discussion and also at congressional hearings where appropriations involving health will be discussed. Furthermore, this special assistant must be selected from among persons who are recognized leaders in the medical field with wide nongovernmental experience. This means a doctor of medicine. This gives medicine a status of dignity and a control over medical affairs, subject only to action of the Secretary. This is a step forward and provides a status never before offered. Naturally, the Board of Trustees did not feel that it could speak for the Association, without the authorization of the House of Delegates in view of the House's previous stand. Hence, the special meeting was called.

Many persons feel that there should be a complete overhauling of the Agency before any change in its status should be approved; however, it should be noted that the reorganization plan affords an opportunity for such an overhauling. One of the great difficulties the new Federal Security Administrator is experiencing is that there are many persons in administrative and policy-making positions in that agency, and also in other departments, who are frozen there by the Civil Service. It has been announced that many of these positions will be unfrozen, thus permitting placing persons in sympathy with the policies of the Administration in policy-making positions.

It was my opinion and the opinion of many other officers of the A. M. A. that we should not oppose this plan but cooperate in making it successful. Of course, we should reserve the right to make recommendations for amendment of the law, should it not prove a satisfactory solution. This, of course, would include an effort to establish a separate department of health, should this appear to be essential. I am glad to say that the House unanimously approved this recommendation, which I believe was a wise decision, in view of all aspects of the situation. Now, if Congress approves, we shall be embarking on a new sea of adventure, and I believe the medical profession of the United States can wield a constructive influence on the health of the American people. I am sure that we shall have every possible cooperation from Washington. The address of the President of the United States to the House of Delegates certainly assured us of that.

LOUIS H. BAUER, M.D., Hempstead, N. Y.

Special Meeting of the House of Delegates



1. Dr. Louis H. Bauer, President of the American Medical Association, welcomes President Eisenhower on arrival at the special meeting of the House of Delegates at Hotel Statler, Washington, D. C., March 14, 1953.

2. and 3. Sen. Robert A. Taft addressing the House of Delegates.

4. Rep. Walter H. Judd addressing the House of Delegates.

5. Mrs. Oveta Culp Hobby and President Eisenhower, with the reception committee: Dr. E. Vincent Askey, Vice Speaker of House of Delegates; Dr. Edward J. McCormick, President-Elect of the American Medical Association; Dr. Dwight H. Murray, Chairman, Board of Trustees; Dr. Elmer L. Henderson, past president of the American Medical Association, and Dr. Louis H. Bauer.

ORGANIZATION SECTION

PRESIDENT EISENHOWER'S MESSAGE

TO THE CONGRESS OF THE UNITED STATES:

I transmit herewith Reorganization Plan No. 1 of 1953, prepared in accordance with the provisions of the Reorganization Act of 1949, as amended.

In my message of February 2, 1953, I stated that I would send to the Congress a reorganization plan defining a new administrative status for Federal activities in health, education, and social security. This plan carries out that intention by creating a Department of Health, Education, and Welfare as one of the executive departments of the Government and by transferring to it the various units of the Federal Security Agency. The Department will be headed by a Secretary of Health, Education, and Welfare, who will be assisted by an Under Secretary and two Assistant Secretaries.

The purpose of this plan is to improve the administration of the vital health, education, and social security functions now being carried on in the Federal Security Agency by giving them departmental rank. Such action is demanded by the importance and magnitude of these functions, which affect the well-being of millions of our citizens. The programs carried on by the Public Health Service include, for example, the conduct and promotion of research into the prevention and cure of such dangerous ailments as cancer and heart disease. The Public Health Service also administers payments to the States for the support of their health services and for urgently needed hospital construction. The Office of Education collects, analyzes and distributes to school administrators throughout the country information relating to the organization and management of educational systems. Among its other functions is the provision of financial help to school districts burdened by activities of the United States Government. State assistance to the aged, the blind, the totally disabled, and dependent children is heavily supported by grants-in-aid administered through the Social Security Administration. The old age and survivors insurance system and child development and welfare programs are additional responsibilities of that Administration. Other offices of the Federal Security Agency are responsible for the conduct of Federal vocational rehabilitation programs and for the enforcement of food and drug laws.

There should be an unremitting effort to improve those health, education, and social security programs which have proved their value. I have already recommended the expansion of the social security system to cover persons not now protected, the continuation of assistance to school districts whose population has been greatly increased by the expansion of defense activities, and the strengthening of our food and drug laws.

But good intent and high purpose are not enough; all such programs depend for their success upon efficient, responsible administration. I have recently taken action to assure that the Federal Security Administrator's views are given proper consideration in executive councils by inviting her to attend meetings of the Cabinet. Now the establishment of the new Department provided for in Reorganization Plan No. 1 of 1953 will give the needed additional assurance that these matters will receive the full consideration they deserve in the whole operation of the Government.

This need has long been recognized. In 1923, President Harding proposed a Department of Education and Welfare, which was also to include health functions. In 1924, the Joint Committee on Reorganization recommended a new department similar to that suggested by President Harding. In 1932, one of President Hoover's reorganization proposals called for the concentration of health, education and recreational activities in a single executive department. The President's Committee on Administrative Management in 1937 recommended the placing of health, education and social security functions in a Department of Social Welfare. This recommendation was partially implemented in 1939 by the creation of the Federal Security Agency—by which action the Congress indicated its approval of the grouping of these functions in a single agency. A new department could not be proposed at that time because the Reorganization Act of 1939 prohibited the creation of additional executive departments. In 1949, the Commission on Organization of the Executive Branch of the Government proposed the creation of a department for social security and education.

The present plan will make it possible to give the officials directing the Department titles indicative of their responsibilities and salaries comparable to those received by their counterparts in other executive departments. As the Under Secretary of an executive department, the Secretary's principal assistant will be better equipped to give leadership in the Department's organization and management activities, for which he will be primarily responsible. The plan opens the way to further administrative improvement by authorizing the Secretary to centralize services and activities common to the several agencies of the Department. It also establishes a uniform method of appointment for the heads of the three major constituent agencies. At present, the Surgeon General and the Commissioner of Education are appointed by the President and confirmed by the Senate, while the Commissioner for Social Security is appointed by the Federal Security Administrator. Hereafter, all three will be Presidential appointees subject to Senate confirmation.

I believe, and this plan reflects my conviction, that these several fields of Federal activity should continue within the framework of a single department. The plan at the same time assures that the Office of Education and the Public Health Service retain the professional and substantive responsibilities vested by law in those agencies or in their heads. The Surgeon General, the Commissioner of Education and the Commissioner of Social Security will all have direct access to the Secretary.

There should be in the Department an Advisory Committee on Education, made up of persons chosen by the Secretary from outside the Federal Government, which would advise the Secretary with respect to the educational programs of the Department. I recommend the enactment of legislation authorizing the defrayal of the expenses of this Committee. The creation of such a Committee as an advisory body to the Secretary will help ensure the maintenance of responsibility for the public educational system in State and local governments while preserving the national interest in education through appropriate Federal action.

After investigation I have found and hereby declare that each reorganization included in Reorganization Plan No. 1 of 1953 is necessary to accomplish one or more of the purposes set forth in section 2(a) of the Reorganization Act of 1949, as amended. I have also found and hereby declare that by reason of these reorganizations, it is necessary to include in the reorganization plan provisions for the appointment and compensation of the new officers specified in sections 1, 2, 3, and 4 of the reorganization plan. The rates of compensation fixed for these officers are, respectively, those which I have found to prevail in respect of comparable officers in the executive branch of the Government.

Although the effecting of the reorganizations provided for in the reorganization plan will not in itself result in immediate savings, the improvement achieved in administration will in the future allow the performance of necessary services at greater savings than present operations would permit. An itemization of these savings in advance of actual experience is not practicable.

DWIGHT D. EISENHOWER
The White House,
March 12, 1953.

REORGANIZATION PLAN NO. 1 OF 1953

Prepared by the President and transmitted to the Senate and the House of Representatives in Congress assembled, March 12, 1953, pursuant to the provisions of the Reorganization Act of 1949, approved June 20, 1949, as amended.

Department of Health, Education, and Welfare

Section 1. *Creation of Department: Secretary.*—There is hereby established an executive department, which shall be known as the Department of Health, Education, and Welfare (hereafter in this reorganization plan referred to as the Department). There shall be at the head of the Department a Secretary of Health, Education, and Welfare (hereafter in this reorganization plan referred to as the Secretary), who shall be appointed by the President by and with the advice and consent of the Senate, and who shall receive compensation at the rate now or hereafter prescribed by law for the heads of executive departments. The Department shall be administered under the supervision and direction of the Secretary.

Sec. 2. *Under Secretary and Assistant Secretaries.*—There shall be in the Department an Under Secretary of Health, Education, and Welfare and two Assistant Secretaries of Health, Education, and Welfare, each of whom shall be appointed by the President by and with the advice and consent of the Senate, shall perform such functions as the Secretary may prescribe, and shall receive compensation at the rate now or hereafter provided by law for under secretaries and assistant secretaries, respectively, of executive departments. The Under Secretary (or, during the absence or disability of the Under Secretary or in the event of a vacancy in the office of Under Secretary, an Assistant Secretary determined according to such order as the Secretary shall prescribe) shall act as Secretary during the absence or disability of the Secretary or in the event of a vacancy in the office of Secretary.

Sec. 3. *Special Assistant.*—There shall be in the Department a Special Assistant to the Secretary (Health and Medical Affairs) who shall be appointed by the President by and with the advice and consent of the Senate from among persons who are recognized leaders in the medical field with wide nongovernmental experience, shall review the health and medical programs of the Department and advise the Secretary with respect to the improvement of such programs and with respect to necessary legislation in the health and medical fields, and shall receive compensation at the rate now or hereafter provided by law for assistant secretaries of executive departments.

Sec. 4. *Commissioner of Social Security.*—There shall be in the Department a Commissioner of Social Security who shall be appointed by the President by and with the advice and consent of the Senate, shall perform such functions concerning social security and public welfare as the Secretary may prescribe, and shall receive compensation at the rate now or hereafter fixed by law for Grade GS-18 of the general schedule established by the Classification Act of 1949, as amended.

Sec. 5. *Transfers to the Department.*—All functions of the Federal Security Administrator are hereby transferred to the Secretary. All agencies of the Federal Security Agency, together with their respective functions, personnel, property, records, and unexpended balances of appropriations, allocations, and other funds (available or to be made available), and all other functions, personnel, property, records, and unexpended balances of appropriations, allocations, and other funds (available or to be made available) of the Federal Security Agency are hereby transferred to the Department.

Sec. 6. *Performance of Functions of the Secretary.*—The Secretary may from time to time make such provisions as the Secretary deems appropriate authorizing the performance of any of the functions of the Secretary by any other officer, or by any agency or employee, of the Department.

Sec. 7. *Administrative Services.*—In the interest of economy and efficiency the Secretary may from time to time establish central administrative services in the fields of procurement, budgeting, accounting, personnel, library, legal, and other services and activities common to the several agencies of the Department; and the Secretary may effect such transfers within the Department of the personnel employed, the property and records used or held, and the funds available for use in connection with such administrative service activities as the Secretary may deem necessary for the conduct of any services so established: *Provided,* That no professional or substantive function vested by law in any officer shall be removed from the jurisdiction of such officer under this section.

Sec. 8. *Abolitions.*—The Federal Security Agency (exclusive of the agencies thereof transferred by section 5 of this reorganization plan), the offices of Federal Security Administrator and Assistant Federal Security Administrator created by Reorganization Plan No. 1 (53 Stat. 1423), the two offices of assistant heads of the Federal Security Agency created by Reorganization Plan No. 2 of 1946 (60 Stat. 1095), and the office of Commissioner for Social Security created by section 701 of the Social Security Act, as amended (64 Stat. 558), are hereby abolished. The Secretary shall make such provisions as may be necessary in order to wind up any outstanding affairs of the Agency and offices abolished by this section which are not otherwise provided for in this reorganization plan.

Sec. 9. *Interim Provisions.*—The President may authorize the persons who immediately prior to the time this reorganization plan takes effect occupy the offices of Federal Security Administrator, Assistant Federal Security Administrator, assistant heads of the Federal Security Agency, and Commissioner for Social Security to act as Secretary, Under Secretary, and Assistant Secretaries of Health, Education, and Welfare and as Commissioner of Social Security, respectively, until those offices are filled by appointment in the manner provided by sections 1, 2, and 4 of this reorganization plan, but not for a period of more than 60 days. While so acting, such persons shall receive compensation at the rates provided by this reorganization plan for the offices the functions of which they perform.

Position Description, Special Assistant to the Secretary (Health and Medical Affairs), Department of Health, Education and Welfare.—The Special Assistant to the Secretary will be the top staff policy adviser to the Secretary with respect to health and medical matters. He will have responsibility for reviewing the health and medical programs throughout the Agency and, where necessary, making recommendations for improvement. On matters of legislative policy where health and medical policies are involved, he will be responsible for making recommendations to the Secretary. This will include review of legislative reports involving health and medical care matters, proposed testimony before Congressional committees relating to health and medical care matters, and other related policy statements such as annual reports, etc.

As chief staff policy adviser in the health and medical field, the Special Assistant to the Secretary will represent the Secretary on top level interdepartmental committees concerned with health and medical care matters, such as the Health Resources Advisory Committee to the President. He will have responsibility for liaison on behalf of the Secretary with important non-governmental groups, such as the American Medical Association, the American Dental Association, the American Hospital Association, the American Public Health Association, and the Association of State and Territorial Health Officers. Such liaison will not, of course, supplant liaison by the constituents of the Department but would be broadly representative of the total interests of the Department in the health field. He will, when appropriate, represent the Secretary in making speeches before various groups interested in health and medical problems faced by the Federal Government and particularly by the Department of Health, Education, and Welfare.

The Special Assistant to the Secretary will, from time to time, represent the Secretary at various international meetings, such as being a delegate to the World Health Assembly of the World Health Organization, and other major international assignments. Such representation will not, of course, supplant appropriate representation from the Public Health Service, the Children's Bureau and other constituents of the Department. The new Department of Health, Education, and Welfare will continue to have major and numerous international responsibilities in the field of health as a positive arm of U. S. foreign policy.

As directed by the Secretary, the Special Assistant to the Secretary will see that related health and medical problems arising in any of the various constituents having health or

medical care programs are properly coordinated. These constituents are: the Public Health Service, the Social Security Administration (including the Children's Bureau), the Food and Drug Administration, the Office of Vocational Rehabilitation and St. Elizabeth's Hospital. Coordination between related activities of these constituents is a matter of very substantial importance.

In short, the Special Assistant to the Secretary will be the top staff policy adviser to the Secretary on health and medical matters, will represent the Secretary in important external relationships of the Department with national and international bodies concerned with health and medical matters, and will, as needed, coordinate related health and medical programs within the Department.

FEDERAL MEDICAL LEGISLATION

Reorganization Plan No. 1: Department of Health, Education, and Public Welfare

President Eisenhower, in Reorganization Plan No. 1, proposes to change the Federal Security Agency into a Department of Health, Education, and Public Welfare with cabinet status (see page 1112). This proposal becomes law within 60 days unless it is disapproved by majority vote of both houses of Congress. Congressman Hoffman (R., Mich.), in H. J. Res. 223, proposes to make Reorganization Plan No. 1 effective within 10 days after enactment of his resolution.

Department of Health, Education, and Public Welfare

Senator Hunt (D., Wyo.), in S. 1215, would reorganize the Federal Security Agency and give it separate cabinet status. A Secretary, an Under Secretary, and four Assistant Secretaries would be appointed by the President and confirmed by the Senate. "An Administrative Assistant Secretary . . . shall be appointed, with the approval of the President, by the Secretary under the classified civil Service." The Secretary would appoint a special advisory commission composed of three leaders from the field of medical science, three from the field of education, and three from the field of social security or public welfare. The commission would meet from time to time to advise, consult with, and make recommendations to the Secretary. The Commissioner of Education and the Surgeon General would continue to carry out their duties as prescribed by law. The title of the Commissioner of Social Security would be changed to Commissioner of Public Welfare, and he would be appointed by the President and confirmed by the Senate. All three would report directly to the Secretary. This measure was referred to the Committee on Government Operations.

Shortening the Period of Service Under the Doctor Draft

Congressman Patterson (R., Conn.) would amend the present "Doctor-Draft law" by H. R. 3706 so that priority 2 physicians would not be required to serve for periods "exceeding (a) 15 months if they have had at least 12 but less than 15 months of active duty in the Army, Air Force, Navy, Marine Corps, Coast Guard, or Public Health Service; (b) 12 months if they have had at least 15 but less than 18 months of such active duty; or (c) 9 months if they have had at least 18 months of such active duty." This measure was referred to the Armed Services Committee.

STATE MEDICAL LEGISLATION

Arkansas

Bills Introduced.—H. 363, proposes the creation of a **board of psychiatric technicians** and defines a psychiatric technician as one who, for compensation or personal profit, (*a*) performs any special service requiring the application of principles of psychiatric treatment based on biological, physical, and social sciences, such as responsible supervision of a patient requiring skill in observation of symptoms and reactions and the accurate recording of facts and carrying out of treatment and medications as prescribed by a licensed physician or psychiatrist, and the application of such technicians' procedures as involved understanding of cause and effect in order to safeguard the life and health of a patient and others, or (*b*) performs such duties as are required in the physical care of a patient and is carrying out medical orders as prescribed by a licensed physician or psychiatrist, requiring an understanding of psychiatric nursing but not requiring the professional service as outlined in (a). S. 489, proposes to prohibit a registered **physical therapist** from treating human ailments by physical therapy or otherwise except under the prescription of a person licensed to practice the healing art.

California

Bill Introduced.—A. C. R. 39, proposes that the governor request the department of public health and department of mental hygiene to make a study of the extent and nature of the problems of alcoholism in the state of California, with particular emphasis on a study of the needs of the cities and counties in establishing effective programs of education, prevention, and rehabilitation and make recommendations for necessary state participation in such programs to the end that the most effective, practical program can be initiated to help reduce the problems of alcoholism within the state of California.

Colorado

Bills Introduced.—H. 260, proposes to make it unlawful for an employer to require any employee or applicant for employment to pay **the cost of a medical examination** or the cost of furnishing any records required by the employer as a condition of employment. S. 162, proposes certain amendments to the **basic science act** among which are including hygiene and sanitation as subjects to be covered by the examination together with the proviso that at the examination no questions concerning any policy, product, or procedure will be asked the use of which by the person being examined in the practice of his profession would constitute a violation of Colorado law.

Connecticut

Bills Introduced.—H. 1231, proposes to allow the free passage of **ambulances** through toll stations on state highways and bridges. H. 1504, proposes the enactment of an **unemployment sickness and disability compensation act.** H. 1527, proposes to authorize nonprofit medical service corporations to furnish medical service through registered **osteopathic physicians** entitled to practice medicine or surgery.

Delaware

Bill Introduced.—S. 92, proposes the enactment of a **temporary disability benefits law.**

Georgia

Bill Introduced.—H. 624, proposes the creation of a Georgia **commission on alcoholism.**

Bills Enacted.—H. 59, has become act no. 251 of the acts of 1953. It provides that no municipal corporation or county authority shall levy or collect any **license or occupational or professional tax upon practitioners of medicine,** osteopathy, chiropractic, dentistry, and other specified professions and occupations. H. 487, has become act no. 485, of the acts of 1953. It is known as the **Georgia postmortem examination act** and provides for the appointment of a medical examiner who shall be a licensed physician designated by the director of the state crime laboratory and the director of the department of public health for the purpose of performing postmortem examinations. S. 34, has become act no. 351 of the acts of 1953. It is a new law providing for the examining and licensing of **practical nurses.**

Hawaii

Bills Introduced.—H. 569, proposes the enactment of a law relating to the commitment and disposition of **sexual psychopaths.** H. 570 and S. 326, propose the creation of a **territorial board of hospitals** to make rules and regulations prescribing schedules of fees and charges for hospital services to be furnished to eligible persons. Every resident of the territory who paid one dollar or more in taxes in the calendar year immediately preceding the year in which hospitalization occurs would be an eligible person. S. J. R. 23, proposes that suppliers of water in the Territory of Hawaii be requested and authorized to enrich the **fluoride content of community water supplies** where the local medical and dental societies approve fluoridation and where the board of health for the Territory of Hawaii approves fluoridation of water supplies as a proper method for that particular community. S. 277, proposes to authorize and direct the board of health to expand its research in the causes, methods of transmitting, treatment, prevention, control, cure, and elimination of leprosy in the Territory.

Idaho

Bills Introduced.—S. 120, proposes enabling legislation relating to the formation and regulations of nonprofit hospital and **medical service corporations.** S. 143, proposes the creation of a **state board of eugenics** to handle matters relating to the sterilization of persons who are feebleminded or ill mentally in such a way that the affliction may cause such persons' progeny to be a menace to society. S. 179, proposes to designate the medical care interim study committee to make a study, investigation, and report, with recommendations to carry out its findings, relating to resources now available in the state concerning the **state medical care needs.**

Bill Enacted.—S. 127, has become ch. 121 of the laws of 1953. It provides for the organization and government of **hospital districts** and imposes upon hospital boards the obligation of acquiring, constructing, improving, and maintaining public hospitals within the districts for the necessary care and treatment of persons requiring hospital services.

The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

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arising in any of the various constituents having health of

Illinois

Bills Introduced.—H. R. 34, proposes the creation of a committee to investigate the need for and the desirability of a state institution for **narcotic addicts.** H. 179, to amend the workmen's compensation act, proposes to authorize an injured **employee to elect to accept the services of a physician,** surgeon, or hospital designated by the employer or to secure his own surgeon or hospital service. In either event, the employer would pay the reasonable cost of providing such services. S. J. R. 5, proposes the appointment of a committee for the purpose of ascertaining the facts of the controversy that has arisen at the University of Illinois concerning **medical research on Krebiozen** and to consider what legislative action if any is necessary or desirable. S. 19, proposes the establishment of an Illinois state **alcoholics hospital** in the city of Chicago. S. 148, proposes to prohibit the sale or offering for **sale of any hypodermic syringe or needle** or any device adaptable to use for intravenal injections to any person other than a licensed physician, a licensed dentist, a licensed veterinarian, or a registered nurse, except on the prescription of a licensed physician.

Indiana

Bills Introduced.—H. 345 proposes the enactment of a **nonoccupational disability act.** H. 455, to amend the workmen's compensation act, proposes to recognize and provide for the right of the **employee to choose his own physician.** S. 38, proposes the appointment of a **commission on alcoholism** to develop and carry out a program for the rehabilitation of alcoholics through the use of medical, psychiatric, and other forms of treatment of chronic alcoholics. S. 205, proposes the creation of a **division of mental health** within the state department of health. The proposal would also create a mental health council to be composed of five members, three of whom shall hold unlimited license to practice medicine, and two of the three would have to be certified by the American Board of Neurology. S. 241, proposes the enactment of a **mental health act,** providing for the detention for observation of persons who appear to be mentally ill and for the admission, treatment, training, commitment, discharge, and release of mentally ill persons. S. 274, proposes the creation of a committee to make a **scientific investigation of chiropractic** to ascertain whether that theory and method of treatment of the sick or injured is a sound and true method and is of any value.

Bill Enacted.—S. 156, has become ch. 53 of the laws of 1953. It makes it the duty of board of school trustees or school commissioners to conduct and administer annually **audiometer tests** or tests of a similar nature with approved scientific instruments or devices for determining the hearing efficiency of school children. Records of such tests must be continuously maintained for the purpose of disclosing any data relating to any child that may assist in diagnosing and treating any auditory abnormality and such diagnosis and treatment shall be upon the recommendation of an examination by a practitioner of the healing arts with unlimited license to practice.

Kansas

Bill Introduced.—H. 449, proposes to authorize the state board of social welfare to establish and equip a treatment center for the study, treatment, and care and research in the methods of treatment of **emotionally, mentally, and socially disturbed children.**

Maine

Bills Introduced.—H. 1094, proposes that any person who treats a human being for a wound apparently caused by the **discharge of a firearm** shall immediately report the same to the county attorney or sheriff. H. 1181, proposes regulations relating to the administering of **medical care** to needy persons 18 years of age or older.

Maryland

Bill Enacted.—H. 216, has become ch. 70 of the laws of 1953. It makes it a misdemeanor for a physician who treats a person for any injury which was caused by or shows evidence of having been caused **by an automobile accident or by a lethal weapon** to fail to report the same to the sheriff of the county, the county police or the state police.

Massachusetts

Bills Enacted.—S. 235, has become ch. 142 of the laws of 1953. It provides that any **medical service corporation** may join with any other medical service corporation organized either under the laws of Massachusetts or any other state for the purpose of establishing or maintaining an agency or corporation designed to facilitate the provision of medical service for residents of the commonwealth employed by firms having employees located in more than one state. S. 236, has become ch. 143 of the laws of 1953. It authorizes **medical service corporations** to contract with a hospital service corporation for a joint or cooperative administration of their affairs and for the joint or cooperative writing and issuing of subscriptions certificates.

Minnesota

Bill Enacted.—S. 361, has become ch. 89 of the laws of 1953. It is an enabling act for the organization of nonprofit **medical service plan** corporations and authorizes such corporations to provide services by duly licensed and registered **doctors of dentistry.**

Missouri

Bill Introduced.—S. 343, proposes that applicants for a license to practice **chiropractic** must show that their chiropractic course covered a period of not less than four years of nine months each and required actual attendance of not less than 4,000 hours.

Montana

Bills Enacted.—H. J. R. 3, was approved March 3, 1953. It provides for the appointment of a committee to survey the methods and facilities now provided in the state for the **training and education of nurses** and to study means by which such training and education may be approved and made available to a greater number of Montana students. H. 327, was approved March 4, 1953. It amended the law relating to **narcotic drugs** by, among other things, providing that a narcotic drug shall be any drug found by the state board of health, after reasonable notice and opportunity for hearing, to have an addiction-forming or addiction-sustaining liability similar to morphine or cocaine.

Nebraska

Bill Enacted.—L. 83, was approved March 6, 1953. It amended the law relating to **narcotic drugs** by defining a narcotic drug as including isonipecaine, amidone, isoamidone, ketobemidone, together with any drug to which the federal laws or regulations relating to narcotic drugs apply and any drug found by the director of the department of health, after reasonable notice and opportunity for hearing, to have addiction-forming and addiction-sustaining liability similar to morphine or cocaine.

Nevada

Bills Introduced.—A. 368, proposes the enactment of a new **Nevada industrial insurance act** to cover industrial injuries and occupational diseases. Among other things, it requires physicians and surgeons who attend a disabled employee to file with the commission a full and complete report of every known disablement to any employee arising out of and in the course of his employment and resulting in loss of life or disability to such person. It also makes it the duty of the physician to inform the disabled workman of his rights under the act and to lend all necessary assistance in making applications for compensation and such proof of other matters as may be required without charge to the worker. S. 175, to amend the law relating to the practice of medicine, proposes that applicants must be **citizens of the United States** or if not citizens must have declared their intention to become a citizen of the United States.

New Jersey

Bills Introduced.—A. 360, proposes the enactment of a **temporary disability benefits law.** A. 396, proposes the creation of a state **medical and dental college.** A. 422, to amend the workmen's compensation act, proposes to authorize employees to make use of the services of **chiropractors.** A. 426, to amend the temporary disability benefits law, proposes to authorize eligible individuals to be cared for by **chiropractors.** A. 441, to amend the workmen's compensation act, proposes to authorize an injured employee to select to treat him any **duly licensed physician.** A. 456, proposes to require the appointment of two **chiropractors to assist the board of medical examiners** in the examination of chiropractic applicants. The proposal would also provide that a licensed chiropractor shall have the right in the examination of patients to use the neurocalometer, x-ray, and other necessary instruments solely for the purpose of diagnosis or analysis, and that no licensed chiropractor shall use endoscopic or cutting instruments or prescribe, administer, or dispense drugs or medicines for any purpose whatsoever or perform surgical operations excepting adjustment of the articulations of the spinal column. S. 202, proposes the creation of a **board of chiropractic examiners** and defines chiropractic as a system of adjusting the articulations of the spinal column by hand only for the correction of a cause of disease. A licensee, under the proposal, would have the right in the examination of patients to use all scientific instruments and x-ray necessary for the purpose of chiropractic spinal analysis; provided, however, that a license to practice chiropractic would not permit the holder to prescribe, administer, or dispense drugs in the examination of a patient or in the treatment of any human ailment, disease, injury, deformity, or mental or physical condition, or to perform surgical operations or to practice obstetrics or to reduce or set fractures or dislocations.

New York

Bills Introduced.—A. 1935, proposes to authorize the state department of health to establish and adopt an adult **hygiene and geriatric program,** designed to improve and protect the health and vitality of middle-aged and elderly citizens of the state. A. 2723, to amend the labor law, proposes to make it unlawful for any employer to require any employee or applicant for employment to pay the **cost of a medical examination** or the cost of furnishing any records required by the employer as a condition of employment. A. 2968, proposes the creation of a temporary commission to study the **rabies control** program.

North Carolina

Bill Introduced.—H. 676, proposes the creation of a **commission on post-mortem medicolegal examinations,** the duties of which, among others, authorizes the state medical examiner to cooperate with all educational institutions and law enforcement agencies of the state for the purpose of furthering medicolegal education and training and for the purpose of establishing and maintaining a central office and laboratory under the supervision of the state medical examiner.

North Dakota

Bills Enacted.—H. 596, was approved March 6, 1953. It amends the the law relating to chiropody by providing that a **doctor of surgical chiropody** is a chiropodist who has a degree from an accredited college of chiropody. It also provides that a doctor of surgical chiropody in addition to other privileges is permitted to practice minor foot surgery and to administer local anesthetic. **Minor foot surgery** shall consist only of any surgical procedure of the foot, except amputation of the foot or amputation of

toe or toes in toto, but does allow partial amputation of toe or toes that can be done under a local anesthetic. S. 88, was approved March 7, 1953. It amends the law relating to **narcotic drugs** by defining a narcotic drug as including drugs to which the federal laws relating to narcotic drugs may now apply; and drugs found by the state laboratories department, after reasonable notice and opportunity for hearing, to have addiction-forming or addiction-sustaining liability similar to morphine or cocaine. S. 111, was approved March 11, 1953. It provides for the examining and licensing of **professional nurses.**

Oklahoma

Bills Introduced.—H. 953, proposes to make it unlawful for any optometrist, physician, or other person doing or purporting or pretending to do eye examination or visual correction to receive or accept any **rebate, kick-back, or reward premium** from any optical company or any other firm or corporation dealing with optical goods, appliances or material. It would also be unlawful for any optometrist, physician, or other person to make eye examination or visual correction in any manner either directly or indirectly as an employee or associate of a person, firm, or corporation not licensed to do eye examinations or visual correction. S. 292, proposes to regulate the **use of the words "college" or "university"** by restricting such use to those agencies offering educational services with the approval of the state board of education, or the Oklahoma State Regents for Higher Education.

Bills Enacted.—H. 538, was approved March 2, 1953. It amends the law relating to **narcotic drugs** by providing that any violation involving a person under the age of 21 years shall be punishable by imprisonment in a penitentiary for not less than 20 years and upon second or subsequent convictions by imprisonment up to and including life. H. 541, was approved Feb. 25, 1953. It authorizes the state board of medical examiners to suspend the license or certificate of a physician when such physician or surgeon becomes **incompetent to practice medicine because of insanity.** H. 545, was approved Feb. 25, 1953. It authorizes the state board of medical examiners to accept and register without examination applicants holding certificates from the **national board of medical examiners.** H. 549, was approved Feb. 25, 1953. It authorizes the board of chiropractic examiners to suspend licenses of chiropractors when such chiropractors have become **incompetent to practice chiropractic because of insanity.**

Oregon

Bill Enacted.—S. 76, has become ch. 45 of the laws of 1953. It requires persons receiving a license to practice **osteopathy** and surgery to file it or a copy thereof with the county clerk of the county wherein such person resides.

Pennsylvania

Bills Introduced.—H. 517, to amend the medical practice act, proposes to require applicants for a license to present evidence indicating that they have served an **internship** of not less than two months in a **state mental hospital.** S. 249, proposes to authorize the department of welfare to establish farms for the care, training, and rehabilitation of **chronic or habitual inebriates.**

South Carolina

Bill Introduced.—H. 1218, proposes to direct the South Carolina Mental Health Commission to set up an **alcoholic rehabilitation center** for the care and treatment of persons suffering from alcoholism.

South Dakota

Bills Enacted.—H. 513, approved March 3, 1953. It requires the **licensing of homes for the aged** under the provisions relating to the licensing of hospitals. H. 767, was approved March 11, 1953. It provides that a state health officer or any superintendent of a county board of health who has information that a person infected with **active tuberculosis** is endangering the health of his family or other persons to direct such person to receive treatment at a specified institution. If the person refuses to do so, the law provides the procedure whereby the person may be committed to the institution by court order. H. 828, was approved March 11, 1953. It authorizes boards of county commissioners to appropriate sums of money annually for the support of public **mental health centers or clinics.** H. 915, was approved March 4, 1953. It relates to the **use of the word "doctor"** and provides, among other things, that only persons who have received the basic science certificate may append to their names the word "doctor" or any contraction thereof or any other word, abbreviation or designation indicating that they are qualified to make diagnosis or treatment.

Tennessee

Bills Introduced.—H. 342, proposes that in any suit in which the plaintiff submits himself to **examination by a physician or surgeon** residing or maintaining an office in the county at the instance of the defendant, either voluntarily or on order of the court, and for which a charge is made or is to be made, it shall be and it is hereby made the duty of the physician or surgeon to furnish the plaintiff with a complete copy of his examination and findings without expense to him. It is further proposed that if said physician is subpoenaed by the plaintiff to appear and testify in open court respecting his examination, he shall be allowed the same fees and mileage provided by law for ordinary and nonexpert witnesses. H. 307, proposes the creation of a **lien in favor of hospitals,** for the value of services rendered by the hospital, upon all causes of action, claims, or demands accruing to the patient on account of injuries for which the care is given. S. 254, proposes to provide for the appointment of **expert witnesses,** proposes that such expert witnesses may be required to testify and proposes that the compensation of such witnesses shall be fixed by the court at a reasonable amount. S. 341, proposes to authorize the board of medical examiners to examine and license applicants desiring to practice **physical therapy** and defines physical therapy as the treatment of any bodily or mental condition of any person by the use of the physical, chemical, and other properties of heat, light, water, electricity, massage, and therapeutic exercise consisting of progressive, relaxation, assistive, resistive and passive movements, exercises for postural defects, breathing exercises, stretching, muscle re-education, coordination and rhythm exercises, exercise by means of mechanical apparatus; ambulation training with or without braces, crutches, or prostheses; and functional training and activities of daily living and including physical rehabilitation procedures. The use of roentgen rays and radium for diagnostic and therapeutic purposes and the use of electricity for surgical purposes, including cauterization, would not be authorized under this proposal.

Texas

Bills Introduced.—H. 513, proposes to make it unlawful for any person to **habitually use narcotic drugs,** be addicted to the use of narcotic drugs, or be under the influence of narcotic drugs, provided that this law would not be applicable to a person who has a medical need for narcotic drugs and who obtains them in accordance with the laws of the state of Texas and of the United States. H. 559, proposes the creation of a **Texas commission on alcoholism** to promote the establishment of constructive programs for treatment aimed at the reclamation, rehabilitation, and successful reestablishment in society of alcoholics. H. 629, proposes an appropriation for equiping, furnishing, and completing the construction of buildings and other permanent improvements at the M. D. Anderson Hospital for **Cancer Research.** S. 183, proposes to regulate the type of **descriptive prefixes and suffixes** that may be used by doctors of medicine, doctors of osteopathy, chiropractors, dentists, optometrists, and chiropodists.

Utah

Bill Introduced.—S. 248, proposes the creation of a **nursing school accreditation board** of review to hear and determine appeals from decisions of the committee coming within the purview of the chapter and relating to the accreditation or disaccreditation of institutions conducting schools of nursing courses for the training of practical nurses.

Bill Enacted.—H. 91, approved March 6, 1953. It provides that **causes of action arising out of physical injury to the person or death,** caused by the wrongful act or negligence of another, shall not abate upon the death of the wrongdoer, and the injured person or the personal representative or heirs of one meeting death, as above stated, shall have a cause of action against the personal representatives of the wrongdoers; provided, however, that the injured person or the personal representatives or heirs of one meeting death shall not recover judgment except upon some competent, satisfactory evidence other than the testimony of the injured person.

Vermont

Bills Introduced.—H. 147, proposes the enactment of a **nursing home licensing law.** H. 278, proposes to provide for the establishment and administration by contract of a **system of health insurance** for state employees. H. 311, proposes an appropriation for the purpose of providing **nursing scholarships.**

West Virginia

Bill Introduced.—S. 340, proposes to make it unlawful for any employer to require any employee or applicant for employment to pay **the cost of a medical examination** or the cost of furnishing any records required by the employer as a condition of employment.

Wisconsin

Bills Introduced.—A. 532, to amend the **narcotic drug act,** proposes that any person may be **compelled to testify** in regard to any violation of the act of which he may have knowledge, even though such testimony may tend to incriminate him, upon being granted immunity from prosecution in connection therewith, and upon the giving of such testimony, said person shall not be prosecuted for or because of the violation relative to which he testified. Any person who refuses to testify after being granted such immunity and sworn as a witness shall be deemed guilty of criminal contempt. A. 626, proposes to define **physiotherapy** as the employment of physical or mechanical instrumentalities with massage, hydrotherapy, electrotherapy, mechanotherapy, and kindred methods of therapy, either directly or indirectly, to the external anatomy of the human body for hygienic or remedial purposes, for purposes of relieving, alleviating, or reducing affected parts thereof, but shall not include reduction of a fracture or dislocation of a bone nor the treatment of a specific disease, except upon the advice of a licensed physician or surgeon. S. 360, proposes the enactment of a **hospital regulation approval act,** the purpose of which is to provide for the development, establishment, and enforcement of standards for the care and treatment of persons in hospitals and standards for the construction and maintenance of hospitals which, in the light of advancing knowledge, will promote safe and adequate treatment of such individuals in hospitals. S. 388, to amend the workmen's compensation act, proposes that whenever a request for examination is made by an employer the commission, upon request of the employee, shall direct any physician the employee shall designate to be present at such examination and join therein and to report his findings and opinion to the employee and the commission. The commission shall pay such physician a reasonable fee and his expenses for the examination and report and for any testimony given before the commission thereon. S. 464, proposes the creation of **liens for hospital, medical, and surgical services** upon insurance policies held by persons to whom such services are rendered S. 1242, to amend the **workmen's compensation act,** proposes to authorize an employee to elect **chiropractic treatment** in cases of back injuries resulting while occupied in the performance of his employment. His selection may be made from a panel of chiropractors named by the employer.

MEDICAL NEWS

CALIFORNIA

Cerebral Palsy Institute.—Under the sponsorship of the United Cerebral Palsy Association of Los Angeles County and the Childrens Hospital of Los Angeles a cerebral palsy institute will be held in Los Angeles April 1-2. Guest speakers will include Drs. George G. Deaver, New York, and Burton Chance, Philadelphia.

Popular Medical Lectures.—The Stanford University School of Medicine, San Francisco, announces the 71st course of popular medical lectures, to be given at Lane Hall (north side of Sacramento Street, near Webster), March 31, April 9, 17, and 27 at 1:30 p. m.:

March 31, Influenza: Past and Present, Ernest Jawetz.
April 9, How to Let Children Grow Up, John A. Anderson.
April 17, Rehabilitation of the Poliomyelitis Patient, William H. Northway.
April 27, Sleep and Sleeping Pills, Windsor C. Cutting.

Breakfast Club.—The Doctors Breakfast Club of the San Fernando Valley Branch of the Los Angeles County Medical Association, which meets Wednesdays at 8 a. m. at St. Joseph's Hospital in Burbank, will hear the following lectures by physicians in April:

April 1, Surgical and Radiological Treatment of Cancer of the Breast, Ian G. Macdonald, Los Angeles.
April 8, Causalgia, Robert W. King, Beverly Hills.
April 15, Diagnosis and Treatment of Malignant Diseases of the Blood, Gurth E. Carpenter, Beverly Hills.
April 22, Prostatism, Carl F. Rusche, Los Angeles.
April 29, Visible Tumors, Clarence E. Nelson, Los Angeles.

COLORADO

Dr. Ebaugh Retires from Professorship.—Dr. Franklin G. Ebaugh, professor of psychiatry at the University of Colorado School of Medicine, and director of Colorado Psychopathic Hospital, Denver, was guest of honor at a dinner given by friends, students, and colleagues in recognition of his retirement after 28 years of service at the school, broken only by service during World War II as a neuropsychiatric consultant to the armed forces, for which he was awarded the Legion of Merit award for distinguished service in the Pacific theater. Dr. Ebaugh was formerly affiliated with the Phipps Clinic, the New Jersey State Hospital, Trenton, and State Reformatory, Philadelphia General Hospital, and the University of Pennsylvania, Philadelphia. An oil painting of Dr. Ebaugh, presented to the school at the dinner, was subsequently hung in the lobby at the Colorado Psychopathic Hospital.

CONNECTICUT

Hartford Hospital Programs.—For its Saturday meetings, held in the amphitheater at 11 a. m., Hartford Hospital presents the following programs in April:

April 4, Idiopathic Pleuropericarditis (and Its Differentiation from Coronary Occlusion), Arthur J. Geiger, New Haven.
April 11, Current Views of Poliomyelitis Control, John R. Paul, New Haven.

Residence for Yale Students.—Yale University, New Haven, has received from the Commonwealth Fund a grant of $2,500,000 for construction of a residence hall for medical students, to be named the Edward S. Harkness Memorial Hall. The building, which will be erected adjacent to the Sterling Hall of Medicine and the Grace-New Haven Community Hospital, will be another unit in the Yale-New Haven Medical Center. Facilities in the residence hall will include rooms for single and married students, lounge, dining hall, recreation rooms, and suites for visiting scientists. Construction will begin next fall.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

FLORIDA

Cancer Cytology Seminar.—The second annual seminar on cancer cytology will be held at Miami, March 30 to April 2. Dr. George N. Papanicolaou, New York, has been invited as guest speaker. Other guest speakers include Joseph K. Cline, Ph.D., director of cancer research, Medical College of Alabama, Birmingham; Dr. Paul F. Fletcher, St. Louis University; and Dr. Lyndon E. Lee, director, Cytology Center, University of Puerto Rico School of Medicine, San Juan. Registration fee, $10. Information may be obtained from the Dade County Cancer Institute, 1155 Northwest 14th St., Miami.

ILLINOIS

Lecture in Winnetka.—On April 1 at 8 p. m. Dr. Herman M. Serota, professor of nervous and mental diseases, Northwestern University Medical School, Chicago, will speak on "Musculoskeletal System" at the North Shore Health Resort, 225 Sheridan Road, Winnetka, in the series of lectures on "Understanding Psychosomatic Disorders." Dr. Serota is research associate of the Institute for Psychoanalysis, Chicago.

Plan Ramp Village for Handicapped.—A public meeting was recently called in Oak Park by the Valiant Development Association, which plans a "village," where homes, apartments, churches, and stores will be built on a one story, ramp plan for paraplegics, cardiac patients, or others who are permanently handicapped. Dwight D. Guilfoil Jr. of Arlington Heights, vice-president of the Paraplegic Manufacturing Company, who is president of the association, says that between 150 and 200 applications have already been received, and plans have been drawn for the first unit including 24 family units (2½ room apartments) and 40 bachelor units (1 room). E. C. Cline, Ph.D., state supervisor, division of vocational rehabilitation, Springfield, addressed the meeting.

Chicago

New Cardiac Group.—The Chicago Heart Association (69 W. Washington St.) announces the formation of a scientific section, membership in which is open to all physician members of the Chicago Heart Association, full-time research workers in the field of cardiovascular disease, pathologists significantly interested in cardiovascular disease, and cardiovascular surgeons. There are no dues.

Meeting on Endocrinology.—The North Side Branch of the Chicago Medical Society will present a panel discussion on "Recent Developments in Endocrinology," April 2, at the Drake Hotel. The program follows:

Trends in Reproductive Physiology, Earl T. Engle, Ph.D., New York.
Estrogenic Therapy in Gynecology, M. Edward Davis, Chicago.
Male Sterility, Roland R. Cross Jr., Chicago.
Some Therapeutic Aspects of Adrenocorticotropin and Cortisone, Richard J. Meyer, Chicago.
Radioactive Iodine, Dwight E. Clark, Chicago.

Reservations may be made through the office of the secretary-treasurer, Dr. Caesar Portes (STate 2-5111).

Cost of Tuberculosis.—A two year study made by Ernest Ni, Ph.D., University of Chicago, indicates that tuberculosis is costing Chicago nearly $100 million a year. The Tuberculosis Institute of Chicago and Cook County sponsored the study. The items considered in Dr. Ni's survey included hospitalization, loss of income during therapy, and loss of further earnings in the cases of those who died, the average total loss in the death of male tuberculosis victims being $63,091, and in the death of women, $37,350. The study, which has been published in pamphlet form, indicates that, had they lived, the 3,820 Chicagoans who died of tuberculosis during the period covered could have earned a total of $161 million, or 35 times the annual expenditure of the Municipal Tuberculosis Sanitarium.

MAINE

Society News.—The Maine Medico-Legal Society announces that, in compliance with a request of the Maine Medical Association to avoid a conflict in meetings, it will not hold its annual meeting in Portland in June. Time and place of the annual medicolegal meeting will be announced at a later date.

April Clinics.—The division of maternal and child health, department of health and welfare, announces a cardiac clinic, in Bangor, April 24, at the Eastern Maine General Hospital 9-11 a. m.; pediatric clinics to be held at the same hospital, April 24, 1:30 p. m. and at the Thayer Hospital in Waterville, April 7, 1:30 p. m.; and orthopedic clinics as follows: Maine General Hospital, Portland, April 13, 9-11 a. m.; Central Maine General Hospital, Lewiston, April 17, 9-11 a. m.; Normal School, Machias, April 1, 1:30-3 p. m.; and Augusta General Hospital, Augusta, April 23, 1-3 p. m.

MARYLAND

Spain Honors Dr. Macht.—In a ceremony at the Spanish Embassy in Washington, D. C., His Excellency José F. De Lequerica, Spanish ambassador to the United States, conferred a diploma and medal on Dr. David I. Macht, research pharmacologist at Sinai Hospital, Baltimore, as a symbol of his election to the Royal Spanish Academy of Pharmacy. The academy, founded in 1589, confers membership on "distinguished scientists for outstanding contributions to human welfare." Of the 40 academicians, 26 are from countries outside Spain. Dr. Macht is the third American so honored, although the academy usually offers membership to only one man in each nation.

Courses in Toxicology.—New courses of study leading to the degrees of master of science in toxicology and doctor of philosophy in toxicology are announced by the Graduate School of the University of Maryland, Baltimore. The courses, which will be given in the department of legal medicine, are open to students who have a bachelor of science degree or its equivalent, with major work in chemistry, including eight semester hours each in general chemistry, organic chemistry, analytical chemistry (both qualitative and quantitative), physical chemistry, physics, and biology, and four semester hours in organic qualitative analysis. Inquiries may be directed to Ronald Bamford, Ph.D., Dean, Graduate School, University of Maryland, College Park, Md., or to Dr. Russell S. Fisher, Professor of Legal Medicine, 700 Fleet St., Baltimore 2.

MASSACHUSETTS

Gynecologic Problems.—On April 1 (2-5 p. m.) as part of its 15 hour Postgraduate Medical Institute course in general medicine, the Massachusetts Medical Society will present the following lectures in the Doctors' Library, Burbank Hospital, Fitchburg:

Common Gynecologic Problems, C. Langdon Parsons, Boston.
Gynecologic Office Problems, Christopher J. Duncan, Brookline.
Prenatal Care and Immediate Management of Late Pregnancy Complications, Daniel J. McSweeney, Boston.

Medical Institute Lectures.—As part of its course in general medicine, the Postgraduate Medical Institute sponsored by the Massachusetts Medical Society offers the following Wednesday lectures (3-5 p. m.) by Boston physicians:

April 1 (Children's Medical Center) Recognition and Management of Hypersensitivity Reactions, Robert P. McCombs, Francis C. Lowell, and James F. Patterson.
April 8 (Peter Bent Brigham Hospital) Metabolic Requirements of Severely Ill Patients, Francis D. Moore, Laura Brooks, John R. Brooks, and David M. Hume.

Dr. Davidson Appointed to Harvard Faculty.—Dr. Charles S. Davidson, who has served on the staff of the Harvard Medical School, Boston, and on the staff of the Thorndike Memorial Laboratory of Boston City Hospital since 1941, has been appointed associate professor of medicine at Harvard Medical School. Dr. Davidson, who resigned as chief of clinical research of the National Institute of Arthritis and Metabolic Diseases in order to accept this position, will continue as associate physician at the Thorndike Memorial Laboratory. He is a member of the A. M. A. Council on Foods and Nutrition and of the Commission on Liver Disease of the Armed Forces Epidemiological Board.

MICHIGAN

Medicolegal Publications.—In April Michigan's medical and legal journals will have issues devoted to medical jurisprudence. Articles by leading Michigan attorneys and medical authors will be printed concurrently in the *Michigan State Bar Journal* and the *Journal of the Michigan State Medical Society*.

The Beaumont Memorial Project.—The February issue of the *Journal of the Michigan State Medical Society* has as its theme the Beaumont Memorial restoration project, conducted by Michigan physicians (*J. A. M. A.* **149:**70 [May 3] 1952). The following articles are included:

To Build a Medical Shrine—Our Privilege, Otto O. Beck, Birmingham.
Financing the Beaumont Memorial, William S. Jones, Menominee.
The Dr. William Beaumont Memorial on Mackinac Island, Alfred H. Whittaker, Detroit.

There is a list of 1,722 physicians who have contributed $22,428.90 to the restoration fund. Pledges and contributions are being received by the Beaumont Memorial Restoration Committee, Box 539, Lansing 3.

MISSOURI

Loeb Lecture.—Alpha Pi chapter of Phi Delta Epsilon sponsored the annual Hanau W. Loeb lecture on "The Need for Iodine," which was given by Dr. James H. Means, Jackson Professor (emeritus) of Clinical Medicine, Harvard Medical School, Boston, March 26 at St. Louis University School of Medicine.

Personal.—In recognition of more than 30 years of practice on the staff of the St. Francis Hospital, Cape Girardeau, Dr. Arthur L. Fuerth was recently given a gold watch by the hospital and staff.——Dr. Ben H. Senturia, assistant professor of clinical otolaryngology, Washington University School of Medicine, St. Louis, recently began his new duties as director of the department of otolaryngology at Jewish Hospital, St. Louis.——Dr. Evarts A. Graham, Bixby professor emeritus of surgery, Washington University School of Medicine, St. Louis, was recently made a chevalier of the French Legion of Honor during a ceremony at the medical school. Presentation of the award by Alfred Weiss, professor of surgery at Strasbourg (France) University, who did graduate work under Dr. Graham some years ago, was followed by a reception in Dr. Graham's honor.

NEW YORK

Dr. Schiff Retires from Health Service.—Dr. Leo F. Schiff, Plattsburg, Vice-President of the American Medical Association, who has served as health officer of Plattsburg City for 25 years and as director of the Clinton County Laboratory, which he established, for 30 years, recently resigned from the health service.

Society News.—The Medical Society of the County of Queens, Inc. (112-25 Queens Blvd., Forest Hills 75) will present a seminar for physicians in general practice, March 28, 10:30 a. m. in the auditorium of the department of health, 125 Worth St., New York. Dr. Justin T. Callahan, New York, will discuss "Psychological Aspects of Pregnancy" and Dr. Harry Bakwin, New York, "Psychological Aspects of Child Care." On March 31 at 9 p. m. the society will hold a meeting in the auditorium, preceded by dinner in the refectory to which members and their wives are invited.

Geriatrics Seminars.—The Albany County Department of Public Welfare will sponsor a series of postgraduate seminars in geriatric medicine at the Ann Lee Home (Shaker Road, R.F.D., Watervliet) on Thursday mornings in April. The course, featuring case demonstrations and therapeutic procedures in geriatric medicine, is open to all physicians and medi-

cal students. On April 2, 10 a. m. to 12:30 p. m., Dr. Marcus B. Einhorn, Albany, will discuss "Geriatric Dermatology." On April 9, 10:30-11:30 a. m., a talk on "Roentgenologic Aspects of Aging" by Dr. Sidney I. Etkin, Albany, will precede a discussion on "Diseases of the Eye," 11:30 a. m. to 12:30 p. m., by Dr. William E. Pickett, Albany. Other lectures will be announced.

New York City

Radio Program.—On April 2 the New York Academy of Medicine will present the following lectures on its FM postgraduate radio program:

Treatment of Diabetic Ketosis and Coma, Edward Tolstoi.
Management of the Enlarged Ovary, Morris A. Goldberger.

Lectures for General Practitioners.—In its Saturday morning seminar the Department of Health of the City of New York will present the following lectures in April:

April 4, Medical Problems of the Older Patient in General Practice, Frederic D. Zeman.
April 11, Prevention and Management of Prematurity, L. M. Hellman, Richard Day.
April 18, Diagnosis and Treatment of Hypertension, George A. Perera.
April 25, Care and Management of the Newborn, Samuel Karelitz.

Symposium on Poliomyelitis.—The Hermann M. Biggs memorial lecture, presented annually at the New York Academy of Medicine under the auspices of the Committee on Public Health Relations, will take the form this year of a symposium on poliomyelitis, which will be held at the monthly stated meeting of the academy, April 2, 8:30 p. m. Dr. Dorothy M. Horstmann, associate professor of preventive medicine, Yale University School of Medicine, New Haven, Conn., will speak on "Epidemiology and Pathogenesis of Poliomyelitis"; Dr. William McD. Hammon, professor of epidemiology and microbiology, Graduate School of Public Health, University of Pittsburgh, on "Passive Immunization Against Poliomyelitis with Especial Consideration of the Effectiveness of Gamma Globulin"; and Herald R. Cox, Sc.D., director, viral and rickettsial research, Lederle Laboratories Division, American Cyanamid Company, Pearl River, on "Active Immunization Against Poliomyelitis."

OKLAHOMA

General Practitioners' Meeting.—At its meeting, March 30, 8 p. m., at the Tulsa Hotel, the Tulsa Academy of General Practice will have as speaker, Dr. George N. Aagaard, dean of Southwestern Medical School of the University of Texas, Dallas, who will discuss "General Practitioners and Medical Education." Dean Aagaard was an associate professor of medicine and director of continuation medical education at the University of Minnesota before assuming his present post.

VIRGINIA

Hospital News.—The annual postgraduate day program of the Memorial and Crippled Children's Hospital, Roanoke, will be held at the Hotel Roanoke, April 1, when the following presentations will be made:

W. Norman Thornton Jr., Charlottesville, Diseases of the Vulva (Kodachrome illustrations).
Kenneth R. Crispell, Charlottesville, and Robert P. Morehead, Winston-Salem, N. C., Clinicopathological Conference.
Robert J. Coffey, Washington, D. C., Chronic Relapsing Pancreatitis.
Joseph F. Ross, Boston, Contribution of Radioactive Isotopes to the Control of Human Disease.

All the speakers will participate in a panel discussion on "Diseases of the Thyroid," with Dr. Crispell as moderator.

WISCONSIN

Course in Internal Medicine.—The University of Wisconsin Medical School, Madison, announces a postgraduate course in advances in internal medicine, April 21-23, State of Wisconsin General Hospital, under the direction of Dr. Ovid O. Meyer. Fee, $10. The course will be limited to 45 registrants. Application should be made promptly to Dr. Robert C. Parkin, University of Wisconsin Medical School, 418 N. Randall Ave., Madison 6.

Bardeen Memorial Lecture.—Dr. Ko K. Chen, professor of pharmacology, Indiana University School of Medicine, Indianapolis, will deliver the annual Bardeen memorial lecture of the Phi Chi medical fraternity at the University of Wisconsin School of Medicine, Madison, April 1.

Lecture on Gynecologic Cancer.—Dr. Clyde L. Randall, professor of obstetrics and gynecology at the University of Buffalo School of Medicine, will be guest speaker at the clinic sponsored by Marquette University School of Medicine Alumni Association March 28 at the medical school. His talk on office diagnosis of gynecologic cancer will be given under the auspices of the American Cancer Society and the Cancer Committee of the Medical Society of Milwaukee County.

GENERAL

Urologists Meet in Havana.—Among the speakers scheduled to address the annual meeting of the Southeastern Section of the American Urological Association at the Hotel Nacional, Havana, Cuba, March 26-29, are Drs. T. Leon Howard, Denver, George Cahill, Elmer Hess, Erie, Pa., Frederic E. B. Foley, St. Paul, and Victor F. Marshall, New York. The Ballenger memorial lecture will be delivered by Homer W. Smith, Sc.D., New York.

Association of Medical Museums.—The annual meeting of the American and Canadian Section of the International Association of Medical Museums will be held at the New Hotel Jefferson, St. Louis, March 31 to April 1. A course in pathological physiology of the lung will be presented on Tuesday, with Dr. Wiley D. Forbus, Durham, N. C., as moderator. The Wednesday afternoon session will include the showing of a movie, "A New Frozen Section Technique." Thirty-one presentations will be made, and four papers will be read by title. Members and guests of the American Association of Pathologists and Bacteriologists, which will hold its meeting in St. Louis, April 2-4, are invited. The annual dinner will be held in conjunction with the pathologists and bacteriologists on Thursday at 7:30 p. m.

Physicians' Art Exhibit.—The American Physicians' Art Association, which will hold its exhibit during the A. M. A. convention in New York, June 1-5, will show about 500 art pieces in 20 different mediums. A gold cup for the best oil landscape is being offered by Wyeth Laboratories; a gold cup for the best piece in the show (Mead Johnson & Company); and a trophy for the most popular art piece (J. Henry Helser & Company). Numerous prizes will be awarded in each medium, and each physician who exhibits will receive a scroll. The art show will be located partly in booth I-27 of the Grand Central Palace, and partly in the Plaza Art Galleries Inc., 9-13 E. 59th St., New York. Winners of trophies will be announced at the art banquet, June 2, 6:30 p. m., at the Hotel Commodore. The banquet ($7 per person) will be informal; members, wives, and friends are cordially invited to attend. Dr. Morris Fishbein, Chicago, will be guest of honor and speaker of the evening. Information may be obtained from Dr. Francis H. Redewill, Secretary, American Physicians Art Association, 1058 Phelan Bldg., San Francisco 2.

Mid-West Cancer Conference.—The annual Mid-West Cancer Conference will be held at the Broadview Hotel, Wichita, Kan., April 2-3. Dr. John P. Berger, Wichita, will preside at the luncheon Thursday, when motion pictures on cancer subjects will be shown. At the informal dinner meeting in the ballroom, 7 p. m., to which ladies are invited, Dr. Cornelius P. Rhoads, New York, will deliver an address on "Horizons in Cancer Research." The Friday morning session will be devoted to a symposium on cancer of the breast with Drs. Cushman D. Haagensen, New York, Juan A. del Regato, Colorado Springs, Colo., and Ernest M. Daland, Boston, as collaborators. A presentation by Dr. Isidore Snapper, Chicago, on "Endocrinological and Metabolic Changes Following Castration and Testosterone Treatment for Breast Cancer," which will open the Friday afternoon session, will be followed by a panel discussion and question period on cancer of the breast. Other guest speakers at the conference, which will be sponsored by

the Kansas Medical Society and the Kansas Division, American Cancer Society, include Drs. Paul C. Bucy, Chicago; William Boyd, Vancouver, British Columbia, Canada; and Henry S. Kaplan, San Francisco.

Meeting of Pathologists and Bacteriologists.—The annual meeting of the American Association of Pathologists and Bacteriologists will be held at the Jefferson Hotel, St. Louis, April 2-4, under the presidency of William H. Feldman, D.V.M., Rochester, Minn. Seventy-six papers will be presented and 11 read by title. The Friday sessions will be devoted to a symposium on "Modification of Structural Changes in Infectious Neoplastic and Other Diseases Following Use of Modern Chemotherapeutic Agents." Dr. Sidney Farber, Boston, and William H. Feldman, D.V.M., Rochester, Minn., will act as referees. The annual dinner, on Thursday, will be preceded by a reception at 6:30 p. m. Reservations for the dinner ($5.50 per person) must be made before Thursday noon. Members and guests of the International Association of Medical Museums are invited to attend the reception and dinner.

Meeting of Anesthesiologists.—The annual meeting of the New England Society of Anesthesiologists, previously scheduled for April 3, will be at the New England Deaconess Hospital in Boston, April 10. The morning session will be devoted to operative clinics at various hospitals. In the afternoon, Boston physicians will present the following program:

Anesthesia for Intracardiac Surgery, William S. Derrick.
Anesthesia for the Diabetic Patient, Priscilla White.
Anesthesia for Oral Surgery, Walter Guralnick, D.D.S., and John C. Sheehan.

"Techniques of Regional Anesthesia," a color sound movie by Drs. John J. Bonica, Tacoma, Wash., and Daniel C. Moore, Seattle, presented through the courtesy of Winthrop-Stearns, Inc., will conclude the afternoon session. The evening meeting will be addressed by Dr. Edward A. Gaensler, Boston, who will speak on "Application of Pulmonary Function Studies to Anesthesia."

Meeting of Plastic Surgeons.—The Pacific Northwest Society of Plastic and Reconstructive Surgery will hold its annual meeting in Vancouver, British Columbia, Canada, March 28 under the presidency of Dr. Adalbert G. Bettman, Portland, Ore. The program will include the following presentations:

Ernest E. Banfield, Tacoma, Wash., Synoviomata.
Alexander H. Bill Jr., Seattle, Free Grafts to the Hand, with a Method to Prevent Finger-Web Contracture.
Walter S. Brown, Seattle, Experiences with Xiphisternal Cartilage.
Carl E. Chism, Seattle, Management of Old Compound Fractures with Soft Tissue Loss.
Robert J. Cowan, Vancouver, B. C., Total Reconstruction of the Eyebrow.
Charles E. Gurney, Portland, Ore., Observations Regarding the Treatment of Hemangiomata.
Verner V. Lindgren, Portland, Ore., Complete Replacement of Facial Skin, Following a Burn (Case Report).
Charles M. MacKenzie, Spokane, Wash., Nasopharyngeal Stenosis.
Rex B. Palmer, Seattle, Keloid and Keloid-Like Scars.
Matthew A. Pilling, Seattle, Care of Decubitus Ulcer (Case Report).
Dan N. Steffanoff, Portland, Ore., Total Reconstruction of Congenital Absence of the Vagina (Case Report).
David E. Sullivan, Spokane, Wash., Face Injuries in Automobile Accidents.
Jan P. Szlazak, Regina, Saskatchewan, Canada, Adamantinoma of Jaw: Treatment and Reconstruction.

CORRECTIONS

Surgical Correction of Lymphedema.—In the article with the foregoing title in THE JOURNAL, March 14, 1953, page 890, left-hand column, the sixth line from the top of the page, and on page 891, right-hand column, the eighth line from the top, the figures in the parentheses should be 0.043 cm.

Corticotropin and the Synthesis of Corticosteroid Hormones.—In the editorial by this title in THE JOURNAL, March 7, 1953, page 823, the fifth sentence in the first paragraph should read "To each of the resulting corticosteroid fractions a calculated weight of crystalline 17-hydroxycorticosterone (hydrocortisone) was added as a carrier."

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ARIZONA:* *Examination.* Phoenix, April 21-23. Sec., Dr. J. H. Patterson, 316 W. McDowell Road, Phoenix.

ARKANSAS:* *Regular. Examination.* Little Rock, June 18-19. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic. Examination.* Little Rock, April 6. Sec., Dr. Carl S. Bungart, 105 North 14th St., Ft. Smith. *Eclectic.* Little Rock, June 4-5. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: San Francisco, June 22-25. Asst. Sec., Mr. Wallace D. Thompson, 1020 N Street, Sacramento 14.

COLORADO:* *Endorsement.* Denver, April 14. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver.

DELAWARE: Dover, July 14-16. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 11-12. Commissioner of Licensure, Dr. Daniel L. Seckinger, 4130 East Municipal Bldg., Washington.

FLORIDA:* Jacksonville, June 28-30. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.

GEORGIA: *Examination.* Atlanta and Augusta, June 9-10. *Reciprocity.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

HAWAII: *Examination.* Honolulu, July 13-15. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, July 13-15. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination.* Chicago, April 7-9. Supt. of Regis., Mr. Frederic B. Selcke, Capitol Bldg., Springfield.

INDIANA: *Examination.* Indianapolis, June 23-25. Ex. Sec., Miss Ruth V. Kirk, 538 K of P Bldg., Indianapolis.

IOWA:* *Examination.* Iowa City, June 15-17. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 10-11. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 8-10. Sec., Dr. Bruce Underwood, 620 South Third St., Louisville 2.

MARYLAND: *Examination.* Baltimore, June 16-19. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, July 14-17. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston 33.

MINNESOTA:* Minneapolis, April 21-23. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: Jackson, June 22-24. Sec., Dr. Felix J. Underwood, Old Capitol Bldg., Jackson 113.

MONTANA: *Examination.* Helena, April 7-8. *Reciprocity.* Helena, April 6. Sec., Dr. S. A. Cooney, 7 West 6th Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEW JERSEY: Trenton, June 16-19. Sec., Dr. Earl S. Hallinger, 28 West State St., Trenton.

NEW MEXICO:* Santa Fe, April 13-14. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NORTH CAROLINA: *Reciprocity.* Pinehurst, May 11. *Examination.* Raleigh, June 22-25. *Reciprocity.* Raleigh, June 23. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 15-17. *Reciprocity.* Columbus, April 7. Sec., Dr. H. M. Platter, 21 W. Broad, Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 10-11. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, July. *Reciprocity.* Portland, April 10-11. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg, Portland.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July. Act. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* Providence, April 2-3. Administrator, Division of Professional Regulation, 366 State Office Bldg., Providence.

SOUTH DAKOTA:* Rapid City, June 17-18. Sec., Dr. C. B. McVay, Yankton Clinic, Yankton.

TEXAS:* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Ft. Worth 2.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City.

VIRGIN ISLANDS: *Examination.* St. Thomas, June 10-11. Sec., Dr. Earle M. Rice, Box 8, St. Thomas.

VIRGINIA: *Examination and Reciprocity.* Richmond, June 18-20. Address: Board of Medical Examiners, 631 First St. S.W., Roanoke.

WEST VIRGINIA: Charleston, April 6-8. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

WYOMING: *Oral. Reciprocity.* Cheyenne, June 8. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARKANSAS: *Examination.* Little Rock, May 5-6. Sec., Mr. Louis E. Gebauer, 1002 Donaghey Bldg., Little Rock.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 20-21. Commissioner of Licensure, Dr. Daniel L. Seckinger, 4130 East Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, June 6. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

MINNESOTA: Minneapolis, April 7-8. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: Omaha, May 5-6. Director, Bureau of Examining Boards, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEVADA: *Examination.* Reno, April 7. Sec., Mr. Frank Richardson, University of Nevada, Reno.

OKLAHOMA: Oklahoma City, April 3. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

SOUTH DAKOTA: *Examination.* Vermillion, June 5-6. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

TEXAS: *Examination.* Galveston, April 17-18. If sufficient number of applications is received from vicinity of Dallas, Austin or Houston, an examination in one of these cities will be given at same time. Chief Clerk, Mrs. Sandra Allen, 407 Perry-Brooks Bldg., Austin.

WASHINGTON: *Examination.* Seattle, July 8-9. Sec., Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN: *Examination.* Madison, April 11. Final date for filing application is April 4. Milwaukee, June 13. Final date for filing application is June 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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* Basic Science Certificate required.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1953 Annual Session, New York, June 1-5.

1953 Clinical Session, St. Louis, Dec. 1-4.

1954 Annual Session, San Francisco, June 21-25.

1954 Clinical Session, Miami, Florida, Nov. 30-Dec. 3.

AERO MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, May 11-13. Dr. Thomas H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Birmingham, April 16-18. Dr. D. L. Cannon, 537 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Areal Meeting, Hotel Statler, Boston, April 20-22. Dr. E. H. Christopherson, 610 Church St., Evanston, Illinois, Executive Secretary.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION, The Atlanta-Biltmore, Atlanta, Ga., April 27-28. Dr. Jack Matthews, 1617 Cathedral of Learning, University of Pittsburgh, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, The Homestead, Hot Springs, Va., May 6-8. Dr. Norris J. Heckel, 122 S. Michigan Blvd., Chicago 3, Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Fort Hayes Hotel, Columbus, Ohio, April 10-12. Dr. Samuel X. Radbill, 7043 Elmwood Ave., Philadelphia 42, Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, Congress Hotel, Chicago, April 6-10. Dr. John Y. Sugg, 1300 York Avenue, New York, Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Hotel Statler, Los Angeles, May 12-16. Dr. Neil A. Dayton, P. O. Box 96, Willimantic, Conn., Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, St. Louis, April 2-4. Dr. Alan R. Moritz, 2085 Adelbert Road, Cleveland 6, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, April 7-9. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN ASSOCIATION FOR THE STUDY OF NEOPLASTIC DISEASES, Lord Baltimore Hotel, Baltimore, April 30-May 2. Dr. Bruce H. Sisler, Gatlinburg, Tenn., Secretary.

AMERICAN ASSOCIATION FOR THORACIC SURGERY, Fairmont Hotel, San Francisco, March 27-30. Dr. Paul C. Samson, 2938 McClure St., Oakland 9, Calif., Secretary.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, Roosevelt Hotel, New Orleans, April 28-29. Dr. Edwin N. Broyles, 1100 North Charles St., Baltimore 1, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Conrad Hilton Hotel, Chicago, April 26-29. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Haddon Hall, Atlantic City, N. J., April 13-17. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 3. Dr. Lawrence E. Hinkle Jr., 525 East 68th St., New York 21, Secretary.

AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., May 1-2. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

AMERICAN GOITER ASSOCIATION, Drake Hotel, Chicago, May 7-9. Dr. George C. Shivers, 100 E. St. Vrain St., Colorado Springs, Colo., Secretary.

AMERICAN HEART ASSOCIATION, Hotel Chelsea, Atlantic City, N. J., April 8-12. Dr. Charles D. Marple, 44 East 23d St., New York 10, Medical Director.

AMERICAN LARYNGOLOGICAL ASSOCIATION, Roosevelt Hotel, New Orleans, April 26-27. Dr. Harry P. Schenck, 326 South 19th St., Philadelphia 3, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Roosevelt Hotel, New Orleans, April 28-30. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

AMERICAN OTOLOGICAL SOCIETY, Roosevelt Hotel, New Orleans, May 1-2. Dr. John R. Lindsay, 950 East 59th Street, Chicago 37, Secretary.

AMERICAN PEDIATRIC SOCIETY, Hotel Traymore, Atlantic City, N. J., May 6-8. Dr. Aims C. McGuinness, 237 Medical Laboratories, University of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN PHYSIOLOGICAL SOCIETY, Conrad Hilton Hotel, Chicago, April 6-10. Dr. E. F. Adolph, Univ. of Rochester School of Medicine and Dentistry, Rochester, N. Y., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Hotel Statler, Los Angeles, May 4-9. Dr. R. Finley Gayle Jr., 6300 Three Chopt Road, Richmond, Va., Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Chalfonte-Haddon Hall, Atlantic City, N. J., April 18-19. Dr. Frederick C. Redlich, 551 Madison Ave., New York 22, Secretary.

AMERICAN RADIUM SOCIETY, Plaza Hotel, St. Louis, April 19-22. Dr. John E. Wirth, 635 Herkimer St., Pasadena 1, Calif., Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, Conrad Hilton Hotel, Chicago, April 6-10. Dr. Elmer H. Stotz, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Chalfonte-Haddon Hall, Atlantic City, N. J., May 4. Dr. William M. M. Kirby, University of Washington School of Medicine, Seattle 5, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, Chicago, April 6-9. Dr. Russell L. Holman, 1542 Tulane Ave., New Orleans 12, Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Cleveland, April 26-29. Dr. Casper M. Epsteen, 25 East Washington St., Chicago 2, Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Conrad Hilton Hotel, Chicago, April 6-10. Dr. Carl C. Pfeiffer, 1853 W. Polk St., Chicago 12, Secretary.

AMERICAN SURGICAL ASSOCIATION, Hotel Statler, Los Angeles, April 1-3. Dr. Nathan A. Womack, Dept. of Surgery, School of Medicine, Univ. of N. C., Chapel Hill, N. C., Secretary.

AMERICAN TRUDEAU SOCIETY, Hotel Statler, Los Angeles, May 18-22. Dr. John D. Steele, 1790 Broadway, New York 19, Secretary.

AMERICAN UROLOGICAL ASSOCIATION, Hotel Jefferson, St. Louis, May 11-14. Dr. Charles H. deT. Shivers, Boardwalk National Arcade Bldg., Atlantic City, N. J., Secretary.

ARIZONA MEDICAL ASSOCIATION, Pioneer Hotel, Tucson, April 26-30. Dr. D. W. Melick, 541 Security Bldg., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Little Rock, April 20-22. Dr. J. J. Monfort, 215 Kelley Bldg., Fort Smith, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Haddon Hall, Atlantic City, N. J., May 5-6. Dr. W. Barry Wood Jr., 600 S. Kingshighway Blvd., St. Louis 10, Secretary.

CONNECTICUT STATE MEDICAL SOCIETY, Hampden High School, New Haven, April 27-29. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Secretary.

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, Blackstone, Congress, Conrad Hilton hotels and Palmer House, Chicago, April 6-10. Dr. M. O. Lee, 2101 Constitution Avenue, Washington 25, D. C., Secretary.

FLORIDA MEDICAL ASSOCIATION, Hollywood Beach Hotel, Hollywood, April 26-29. Dr. Samuel M. Day, 413 Professional Bldg., Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Savannah, May 10-13. Dr. David H. Poer, 875 West Peachtree St. N.E., Atlanta, Secretary.

HAWAII TERRITORIAL MEDICAL ASSOCIATION, Island of Maui, April 30-May 3. Dr. Samuel L. Yee, 1163 South Beretania St., Honolulu, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 19-22. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Los Angeles, April 21-24. Dr. Arthur K. Peterson, 350 East 22d St., Chicago 16, Secretary.

IOWA STATE MEDICAL SOCIETY, Des Moines, April 26-29. Dr. Allan B. Phillips, 529 36th St., Des Moines 12, Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Ala., April 12-18. Dr. Eugene H. Dibble Jr., Tuskegee Institute, Ala., Secretary.

KANSAS MEDICAL SOCIETY, Wichita, May 4-7. Dr. Dale D. Vermillion, 315 West Fourth St., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Roosevelt Hotel, New Orleans, May 7-9. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 28-29. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 19-21. Dr. Robert W. Buck, 22 The Fenway, Boston 15, Acting Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Biloxi, May 11-14. Mr. Roland B. Kennedy, 508 First Federal Bldg., Jackson, Executive Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Kansas City, April 26-29. Dr. H. E. Petersen, 634 N. Grand Blvd., St. Louis 3, Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Statler and Biltmore hotels, Los Angeles, May 18-22. Mr. Kemp D. Battle, 1790 Broadway, New York 19, Secretary.

NEBRASKA STATE MEDICAL ASSOCIATION, Paxton Hotel, Omaha, May 11-14. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln 8, Secretary.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS, Boston, April 10. Dr. Francis J. Audin, 114 Danehill Rd., Newton Highlands 61, Mass., Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Haddon Hall, Atlantic City, May 18-21. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Hilton Hotel, Albuquerque, May 7-9. Dr. T. E. Kircher Jr., 221 West Central Ave., Albuquerque, Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, Buffalo, May 4-8. Dr. Walter P. Anderton, 386 Fourth Avenue, New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 10-13. Dr. Millard D. Hill, 203 Capital Club Bldg., Raleigh, Secretary.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Clarence Parker Hotel, Minot, May 9-12. Dr. E. H. Boerth, Box 1198, Bismarck, Secretary.

NORTH PACIFIC SOCIETY OF NEUROLOGY AND PSYCHIATRY, Portland, Ore., April 10-11. Dr. Robert A. Coen, 218 Mayer Bldg., Portland 5, Ore., Secretary.

OGDEN SURGICAL SOCIETY, Orpheum Theater, Ogden, Utah, May 20-22. Dr. Irwin B. McQuarrie, 401 Eccles Bldg., Ogden, Utah, President.

OHIO STATE MEDICAL ASSOCIATION, Netherland Plaza, Cincinnati, April 21-23. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

OKLAHOMA STATE MEDICAL ASSOCIATION, Cimarron Ballroom, Tulsa, April 13-15. Mr. R. H. Graham, 1227 Classen Drive, Oklahoma City, Executive Secretary.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY, Los Angeles, April 24-28. Dr. H. P. House, 1136 West 8th St., Los Angeles 14, Secretary.

RHODE ISLAND MEDICAL SOCIETY, Providence, May 6-7. Dr. Thomas Perry Jr., 106 Francis Street, Providence, Secretary.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

LOS ANGELES, Statler Hotel, March 30-31. Dr. Ewing L. Turner, 1930 Wilshire Blvd., Los Angeles, Chairman.

CALGARY, Alberta, Canada, Palliser Hotel, April 23-24. Dr. Donald G. MacQueen, Colonel Belcher Hospital, Calgary, Alberta, Canada, Chairman.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Hotel Statler, Los Angeles, May 3. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 5, Secretary.

SOCIETY OF CLINICAL SURGERY, Spring Meeting, Nashville, Tenn., May 1-2. Dr. Champ Lyons, 620 South 20th St., Birmingham 5, Ala., Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, Hotel Traymore, Atlantic City, N. J., May 4-6. Dr. Sydney S. Gellis, 330 Brookline Ave., Boston 15, Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Columbia Hotel, Columbia, May 4-7. Dr. Robert Wilson Jr., 120 W. Cheves St., Florence, Secretary.

SOUTHEASTERN ALLERGY ASSOCIATION, Andrew Jackson Hotel, Nashville, Tenn., May 15-16. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 1, S. C., Secretary.

TENNESSEE STATE MEDICAL ASSOCIATION, Peabody Hotel, Memphis, April 13-15. Mr. V. O. Foster, 504 Doctors Bldg., Nashville, Executive Secretary.

TEXAS MEDICAL ASSOCIATION, Shamrock Hotel, Houston, April 26-29. Mr. N. C. Forrester, 1801 Lamar Blvd., Austin, Executive Secretary.

U. S. CHAPTER, INTERNATIONAL COLLEGE OF SURGEONS, SURGICAL DIVISION MEETINGS:

ST. LOUIS, Statler Hotel, March 31-April 1. Dr. Roland Klemme, 4952 Maryland Ave., St. Louis 8, Chairman.

KNOXVILLE, TENN., Andrew Johnson Hotel, April 24-25. Dr. E. Park Niceley, Acuff Clinic, 514 West Church St., Knoxville, Tenn., Chairman.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Hotel Statler, Los Angeles, April 18-25. Dr. E. P. Luongo, General Petroleum Corp., 613 South Flower St., Los Angeles 14, Secretary.

WESTERN SECTION AMERICAN UROLOGICAL ASSOCIATION, Palace Hotel, San Francisco, April 27-30. Dr. Howard J. Hammer, 908 Hyde St., San Francisco 9, Chairman.

WESTERN SOCIETY OF ELECTRO-ENCEPHALOGRAPHY, Hotel Statler, Los Angeles, May 9-10. Dr. Sylvester N. Berens, 902 Boren Ave., Seattle, Secretary.

FOREIGN

BRITISH MEDICAL ASSOCIATION, Cardiff, S. Wales, July 13-17. Dr. A. MaCrae, B. M. A. House, Tavistock Square, London W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Winnipeg, Manitoba, Canada, June 15-19. Dr. T. C. Routley, 135 St. Clair Avenue W., Toronto 5, Ontario, Canada, General Secretary.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Chateau Frontenac, Quebec, Canada, October 26-29. Dr. A. William Friend, 515 Nome Ave., Akron 20, Ohio, Chairman, Program Committee.

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF ANGIOLOGY, Lisbon, Portugal, Sept. 18-20. Dr. Henry Haimovici, 105 East 90th St., New York 28, N. Y., U. S. A., Secretary.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 14-20. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

EUROPEAN CONGRESS OF ALLERGOLOGY, Copenhagen, Denmark, May 20-23. Dr. Egon Brunn, Gersonavej 8, Hellerup, Copenhagen, Denmark, Secretary General.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF AUDIOLOGY, Leiden, Netherlands, June 5-6. Dr. H. A. E. ve Dishoeck, Leiden University, Leiden, Netherlands, President.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF THE EUROPEAN SOCIETY OF HAEMATOLOGY, Amsterdam, Holland, Sept. 8-12. Dr. M. C. Verloop, Maliesingle 15, Utrecht, Holland, Secretary.

INTERNATIONAL CONGRESS ON GENETICS, Bellagio, Italy, August 4. Prof. C. Barigozzi, Instituto de Genetica, Universita de Milano, 10 via Celoria, Milan, Italy, Secretary.

INTERNATIONAL CONGRESS OF GYNECOLOGY, Geneva, Switzerland, July 21-26, 1954. Dr. Maurice Fabre, 1, rue Jules-Lefebore, Paris IXe, France, General Secretary.

INTERNATIONAL CONGRESS OF HIPPOCRATIC MEDICINE, Evian, France, Sept. 3-6. Prof. P. Delore, 13 rue Jarente, Lyons, France, Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Sao Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U.S.A., Secretary-General

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept. 6-12. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 20-24, 1954. For information write: Prof. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Bologna, Italy, May 3-7. Dr. Guiseppe Cristini, Clinica Oculistica, Policlinico, Bologna, Italy, General Secretary.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-13. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Havana, Cuba, Oct. 12-17. Prof. Felix Hurtado, 5a Avenue 124, Miramar, Havana, Cuba. President.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K, Denmark, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL FERTILITY ASSOCIATION, Henry Hudson Hotel, New York, N. Y., U. S. A., May 25-31. Dr. Abner I. Weisman, 1160 Fifth Avenue, New York 29, N. Y., U. S. A., Associate Secretary General.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL GYNAECOLOGICAL MEETING, Paris, France, May 22-23. For information write: Dr. Jacques Courtois, 1, rue Racine, St. Germain-en-Laye, Seine et Oise, France.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL LEPROSY CONGRESS, Madrid, Spain, Oct. 3-10. Dr. Felix Contreras, Moreto 15, Madrid, Spain, Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL PSYCHO-ANALYTICAL CONGRESS, Bedford College, Regent's Park, London N.W.1, England, July 26-30. Dr. Ruth S. Eissler, 285 Central Park West, New York 24, N. Y., Hon. Secretary.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

PACIFIC SCIENCE CONGRESS, Quezon City and Manila, Philippines, Nov. 16-28. Dr. Patrocinio Valenzuela, College of Pharmacy, University of the Philippines, Quezon City, Philippines, Secretary-General.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

PHILIPPINE MEDICAL ASSOCIATION, Manila, April 19-26. Dr. Manuel D. Penas, Doctor's Hospital, 707 Vermont St., Manila, Philippines, Secretary.

ROYAL SANITARY INSTITUTE HEALTH CONGRESS, Hastings, England, April 28-May 1. For information write: Secretary, Royal Sanitary Institute, 90 Buckingham Palace Road, London 5, W1, England.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 22-29. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICAL THERAPY, London, England, Sept. 7-12. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, The Hague, Netherlands, Aug. 31-Sept. 7. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary-General.

DEATHS

Clark, Cyrus J. ⊕ Indianapolis; born in Carmel, Ind., Nov. 16, 1900; Indiana University School of Medicine, Indianapolis, 1923; clinical professor of cardiology at his alma mater, where he was chairman of the department of medical economics and postgraduate instruction; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the American Heart Association and the Indiana Heart Foundation; during World War II in command of the Army General Hospital 32, recruited and sponsored by the Indiana University School of Medicine; chief of medical staff and chief of vascular disease clinics, Indianapolis General Hospital; on the visiting staff, Methodist and St. Vincent's hospitals; senior consultant, VA Hospital; died in the Riverview Hospital, Noblesville, Jan. 22, aged 52, of injuries received in an automobile accident.

Shanks, Edgar De Witt ⊕ Atlanta, Ga.; born in Banks, Ala., in 1889; Atlanta College of Physicians and Surgeons, 1913; for 16 years secretary-treasurer of the Medical Association of Georgia and editor of the association's journal; served on numerous committees of the Fulton County Medical Society and was elected to its presidency in 1935; member of the House of Delegates of the American Medical Association in 1946; at one time assistant professor of clinical medicine at Emory University School of Medicine; served overseas during World War I; affiliated with Piedmont, St. Joseph's, Georgia Baptist, and Crawford W. Long hospitals; on July 1, 1951, more than 50 friends presented him with a silver service in appreciation of his "faithful and loyal service to medicine in Georgia"; died Feb. 12, aged 63, of myocardial infarction and chronic congestive heart failure.

Williamson, Charles Ready ⊕ Newton, Mass.; born in Auburn, Maine, Nov. 26, 1916; Harvard Medical School, Boston, 1942; assistant in medicine at his alma mater; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; for three years during World War II served in the U. S. Navy as a medical officer aboard a destroyer in the Pacific theater of operations; awarded the Bronze Star medal for rescuing wounded men from a sinking vessel and for his work with the survivors in the sea awaiting rescue and later aboard the rescue vessels; affiliated with Newton-Wellesley Hospital in Newton, Faulkner and Boston City hospitals in Boston, and Brooks Hospital in Brookline; died Jan. 13, aged 36.

Fuller, Solomon Carter, Framingham, Mass.; born in Monrovia, Liberia, in 1872; Boston University School of Medicine, 1897; professor emeritus of neurology at his alma mater; member of the American Psychiatric Association and New England Society of Psychiatry; in 1943 was awarded a doctor of science degree from Livingstone College of Salisbury, N. C., for his outstanding work in psychiatry; for many years affiliated with Westboro (Mass.) State Hospital, Massachusetts Memorial Hospital in Boston, and the Framingham Union Hospital, where he died Jan. 16, aged 81, of diabetes mellitus and gastrointestinal malignancy.

Larsen, Carl Levin ⊕ St. Paul; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1904; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past president of the Ramsey County Medical Society; affiliated with Miller, St. Luke's, and Bethesda hospitals and Gillette State Hospital for Crippled Children; died Jan. 29, aged 71, of coronary occlusion.

Bailey, Cornelius Oliver ⊕ Los Angeles; born in Quinlan, Texas, Feb. 11, 1887; University of Texas School of Medicine, Galveston, 1915; emeritus professor of radiology at the College of Medical Evangelists; specialist certified by the American Board of Radiology; fellow of the American College of Physicians; at one time an officer in the regular army; served as surgeon general of the Military Order of the World Wars; affiliated with Beverly Community Hospital in Montebello and the White Memorial Hospital, where he died Feb. 1, aged 65, of hypertensive cardiovascular disease and arteriolar nephrosclerosis.

Clough, Francis Edgar ⊕ San Bernardino, Calif.; Rush Medical College, Chicago, 1902; member of the Western Surgical Association; fellow of the American College of Surgeons; was past president of the South Dakota Medical Association, South Dakota Hospital Association, and a member of the state board of medical examiners; affiliated with St. Bernardine's Hospital and San Bernardino County Charity Hospital; at one time physician in charge of Homestake Hospital in Lead, S. D.; killed in an automobile accident in Laguna Beach, Feb. 9, aged 75.

Sherwin, Charles Frederick ⊕ St. Louis; born in Glasgow, Ill., in 1885; St. Louis University School of Medicine, 1914; associate professor of surgery at his alma mater; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; served as president of the John A. Andrew Clinical Society; chief surgeon and medical director of the police department; affiliated with Barnard Free Skin and Cancer Hospital, St. Mary's Group of Hospitals, and St. Louis City Hospital; died Feb. 12, aged 68, of heart disease.

Abrams, Marc Victor, Miami Beach, Fla.; Long Island College Hospital, Brooklyn, 1913; died in Mount Sinai Hospital Dec. 18, aged 62, of cerebral hemorrhage, arteriosclerosis, and hypertension.

Austin, Lewis King, Portland, Maine; Jefferson Medical College of Philadelphia, 1894; died Oct. 21, aged 83, of pneumonia and arteriosclerosis.

Autenreith, William Clifford ⊕ Youngstown, Ohio; University of Pennsylvania School of Medicine, Philadelphia, 1910; died in South Side Hospital Dec. 31, aged 65, of coronary thrombosis.

Babbitt, Charles Holton ⊕ Nashua, N. H.; University of the South Medical Department, Sewanee, Tenn., 1901; died in Newton-Wellesley Hospital in Newton, Mass., Nov. 27, aged 83, of cancer.

Babcock, Harold Lester ⊕ Dedham, Mass.; Boston University School of Medicine, 1910; professor of otology at his alma mater; fellow of the American College of Surgeons; affiliated with Massachusetts Memorial Hospitals in Boston; died Jan. 21, aged 67, of carcinoma.

Barksdale, Lee Scott ⊕ Hopewell, Va.; Medical College of Virginia, Richmond, 1937; secretary-treasurer of the Fourth District Medical Society; served during World War II; formerly health officer; died in the Medical College of Virginia Hospital Division, Richmond, Jan. 28, aged 40, of congestive heart failure.

Barr, William Hunter ⊕ Wells, Minn.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; died in St. Peter State Hospital in St. Peter Dec. 27, aged 73, of Parkinsonism, cerebral arteriosclerosis and congestive heart failure.

Boyd, John Otto ⊕ Roanoke, Va.; University College of Medicine, Richmond, 1905; member of the South Atlantic Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; formerly vice-president of the Medical Society of Virginia; served as president of the Roanoke Academy of Medicine; affiliated with Roanoke Hospital; died Jan. 1, aged 71, of coronary disease.

⊕ Indicates Member of the American Medical Association.

Bruce, John Angus ⊕ Quincy, Mass.; University of the City of New York Medical Department, New York, 1893; served on the staffs of the Whidden Memorial Hospital in Everett, Malden (Mass.) Hospital, and the Lawrence Memorial Hospital in Medford; died Jan. 13, aged 94, of senility.

Buckner, William Thomas, Shelbyville, Ky.; University of Louisville Medical Department, 1893; served as county health officer and as a member of the city council and city school board; died Feb. 1, aged 86, of arteriosclerosis.

Burns, Robert William ⊕ Green Bay, Wis.; Marquette University School of Medicine, Milwaukee, 1930; member of the American Trudeau Society and the American Academy of General Practice; died Dec. 1, aged 48, of pulmonary embolism following an automobile accident.

Bush, Earl Blaine ⊕ Ames, Iowa; Drake University College of Medicine, Des Moines, 1908; past president of the Iowa State Medical Society; affiliated with Iowa State College Hospital; died Jan. 14, aged 68, of coronary occlusion.

Butterfield, Rupert Olin, Denver; Denver College of Physicians and Surgeons, 1901; served on the staff of the Denver General Hospital; for many years on the staff of St. Anthony's Hospital; died in Sedalia, Colo., Jan. 5, aged 86.

Caulk, William H., Lincoln, Neb.; College of Physicians and Surgeons, Keokuk, Iowa, 1881; died in St. Elizabeth Hospital Dec. 29, aged 97, of acute cardiac failure.

Charbonneau, Lionel Charles, Brooklyn; Bellevue Hospital Medical College, New York, 1888; died Feb. 5, aged 85, of angina pectoris.

Cross, Grace Ella, Boston; Boston University School of Medicine, 1886; formerly affiliated with Massachusetts Homeopathic Hospital; died Jan. 29, aged 89.

Daghir, Nejm Moses Abu ⊕ St. Marys, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1919; past president and secretary of the Elk-Cameron Counties Medical Society; physician for St. Mary's High School; on the staff of the Kaul Memorial Hospital; died Jan. 30, aged 64, of a heart attack.

Daniell, Anthony Wingrove ⊕ Drexel Hill, Pa.; Jefferson Medical College of Philadelphia, 1898; died Nov. 25, aged 90.

Dedolph, Theodore Hubert ⊕ Braham, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1912; died in VA Hospital, St. Cloud, Dec. 22, aged 63.

Elsen, Matt ⊕ Winnebago, Ill.; Northwestern University Medical School, Chicago, 1917; served during World War I; for 15 years member of the Winnebago Consolidated School Board, and for several years school treasurer in the township; affiliated with Swedish American Hospital and the Rockford Memorial Hospital in Rockford, where he died Nov. 2, aged 65, of hemorrhage from duodenal ulcer and carcinoma of the urinary bladder.

Emmons, Henry Manning ⊕ Boston; Boston University School of Medicine, 1902; professor emeritus of clinical ophthalmology at his alma mater; specialist certified by the American Board of Ophthalmology; member of the New England Ophthalmological Society; affiliated with Faulkner and Massachusetts Memorial hospitals; died Jan. 19, aged 76, of cerebral arteriosclerosis and pneumonia.

Fair, Baxter Beach, Detroit; University of Michigan Medical School, Ann Arbor, 1928; member of the American Psychiatric Association; died Jan. 8, aged 50, of heart disease.

Falkner, Lewis William, Youngstown, N. Y.; Baltimore Medical College, 1907; died in the VA Hospital, Buffalo, Nov. 4, aged 70, of myocardial infarction.

Fannaff, Frederic Leonard, Elk Rapids, Mich.; Detroit College of Medicine, 1909; president of the library board; formerly practiced in Grand Rapids, where he was on the visiting staffs of St. Mary's, Butterworth, and Blodgett Memorial hospitals; on the visiting staff of James Decker Munson Hospital of Traverse City and the Little Traverse Hospital in Petoskey; died Dec. 29, aged 70, of aneurysm of the abdominal aorta.

Ferguson, Andrew Ross, Orland Park, Ill.; Northwestern University Medical School, Chicago, 1949; served during World War II; died Feb. 20, aged 29.

Fogg, Edward Samuel ⊕ Corcoran, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1897; an Associate Fellow of the American Medical Association; died Dec. 26, aged 85.

Fry, Elma May ⊕ Dallas, Texas; Rush Medical College, Chicago, 1927; formerly on the faculty of Southwestern Medical School of the University of Texas; fellow of the American College of Surgeons; affiliated with Methodist, Medical Arts, Baylor University, St. Paul's, Gaston, and Parkland hospitals; died Dec. 17, aged 65, of coronary occlusion.

Geismar, Simon ⊕ New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1911; served during World War I; affiliated with Hotel Dieu, Sisters Hospital; died in Touro Infirmary Jan. 4, aged 65, of cancer.

Gerin, Edward Thomas, Norfolk, Neb.; University of Nebraska College of Medicine, Omaha, 1937; resident physician at Norfolk State Hospital; died Dec. 21, aged 43, of myocarditis.

Golding, C. C., Wichita, Kan.; Gate City Medical College, Dallas, Texas, 1906; died Jan. 11, aged 87, of hypostatic pneumonia.

Gowens, Henry Lytle Jr. ⊕ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1908; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; affiliated with Philadelphia General and Mercy-Douglas hospitals; died in Hahnemann Hospital Jan. 2, aged 68, of coronary thrombosis.

Gray, Andrew J. ⊕ Comanche, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1896; died in Blackwell Sanitarium, Gorman, Dec. 24, aged 90, of cerebral hemorrhage.

Green, Peter Charles, Philadelphia; Jefferson Medical College of Philadelphia, 1893; died in Germantown Hospital Jan. 5, aged 79, of lobar pneumonia.

Gruetzner, Edward Theodore, Fairchance, Pa.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1916; died in the Uniontown (Pa.) Hospital Nov. 7, aged 65.

Harman, Eugene Paul, Brooklyn; New York University Medical College, New York, 1896; for many years supervising medical inspector for the board of health; formerly on the courtesy staff of Carson C. Peck Memorial Hospital; died in Brooklyn Hospital Jan. 19, aged 79, of coronary thrombosis.

Hartman, Harry Miller ⊕ Gettysburg, Pa.; Baltimore Medical College, 1902; served on the staff of the Annie M. Warner Hospital; ex-assemblyman; died Jan. 14, aged 79.

Healey, Eugene Joseph ⊕ Mamaroneck, N. Y.; University and Bellevue Hospital Medical College, New York, 1911; served on the staff of the United Hospital in Port Chester; died Jan. 13, aged 65, of arteriosclerotic heart disease.

Heffernan, John Francis, Carleton, Mich.; Vanderbilt University School of Medicine, Nashville, Tenn., 1916; died in Providence Hospital in Detroit Jan. 2, aged 76, of uremia.

Holloway, Ellis Welcome ⊕ Tampa, Fla.; Atlanta College of Physicians and Surgeons, 1911; affiliated with St. Joseph's and Tampa Municipal hospitals; died Jan. 14, aged 71, of arteriosclerotic heart disease.

Hoyt, George Edgar ⊕ Menomonee Falls, Wis.; Northwestern University Medical School, Chicago, 1892; past president of the Waukesha County Historical Society; at one time deputy state health officer, served in the state assembly and in the senate; died Jan. 16, aged 91, of chronic myocarditis.

Kingsbury, Oscar J. ⊕ Steelton, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1909; served during World War I; died in the Harrisburg (Pa.) Hospital Dec. 11, aged 68, of obstructive jaundice.

⊕ Indicates Member of the American Medical Association.

Mott, Albert Elgin ⊕ Buffalo; University of Buffalo School of Medicine, 1905; died in Millard Fillmore Hospital Jan. 5, aged 78, of acute renal insufficiency.

Mueller, William, Jacksonville, Fla.; Eclectic Medical College of the City of New York, 1893; died Dec. 30, aged 83, of carcinoma of the prostate.

Muir, Donald Cameron, Greensburg, Pa.; George Washington University School of Medicine, Washington, D. C., 1940; served during World War II; formerly affiliated with VA Hospital in New York City; died Jan. 26, aged 39, of cerebral embolism.

Neal, William Joel, Drumright, Okla.; University of Nashville Medical Department, 1905; died Jan. 24, aged 80, of myocarditis and nephritis.

Newton, William Brown ⊕ Glendale, Calif.; University of Nashville (Tenn.) Medical Department, 1901; member of the Kansas Medical Society; formerly on the staff of St. Joseph's Hospital in Concordia, Kan.; died Jan. 7, aged 74, of adenocarcinoma of the colon.

Norton, Francis P., Rochester, Minn.; Chicago College of Medicine and Surgery, 1905; died Dec. 24, aged 65, of cirrhosis of the liver.

Oppegaard, Manford O. ⊕ Crookston, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1910; formerly secretary of the Red River Valley Medical Society; at one time mayor; affiliated with Bethesda and St. Francis hospitals; chairman of the board, Sunnyrest Sanatorium; died Jan. 22, aged 67, of coronary occlusion.

Pelikan, Charles Carl ⊕ Lincoln, Neb.; University of Nebraska College of Medicine, Omaha, 1928; member of the American Academy of General Practice; affiliated with Bryan Memorial and St. Elizabeth's hospitals; medical examiner for the Chicago, Baltimore and Ohio Railroad; died Jan. 19, aged 56, of acute coronary occlusion.

Powers, Joseph Clinton ⊕ Hampton, Iowa; Rush Medical College, Chicago, 1897; at one time mayor of Hampton; fellow of the American College of Surgeons; served on the staff of the Lutheran Hospital, where he died Jan. 5, aged 84, of pneumonia.

Precht, Edward, Ridgewood, N. Y.; Long Island College Hospital, Brooklyn, 1905; at one time an inspector for the department of health of New York City; practiced in Brooklyn, where he was affiliated with Wyckoff Heights Hospital and Bethany Deaconess Hospital, where he died Jan. 30, aged 69, of brain tumor.

Rayl, Claudius Caesar ⊕ Decatur, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; past president of the Twelfth District Medical Society; affiliated with Adams County Memorial Hospital, where he died Jan. 3, aged 71, of cerebral thrombosis.

Reesor, Otter Robinson ⊕ Louisville, Ky.; Louisville Medical College, 1901; served during World War I; formerly mayor of Campbellsville; at one time medical director of the state workmen's compensation board; died Jan. 21, aged 73, of carcinoma.

Robbins, Allen Williams, Minneapolis; Denver College of Medicine, 1901; died in St. Barnabas Hospital Dec. 4, aged 78, of cardiac decompensation.

Roseman, Milo A. J. ⊕ Philadelphia; Jefferson Medical College of Philadelphia, 1925; affiliated with Frankford Hospital, Nazareth Hospital, Abington Hospital, and Jeanes Hospital, where he died Jan. 27, aged 55, of arteriosclerotic heart disease.

Ross, Louis Francisco ⊕ Richmond, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; member of the American Psychiatric Association; formerly medical superintendent of the Richmond State Hospital; affiliated with Reid Memorial Hospital; at one time assistant surgeon of the Pennsylvania Railroad; died Jan. 29, aged 72, of hypertensive heart disease.

Scala, Norman Philip ⊕ Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1920; member of the Association for Research in Ophthalmology; died Jan. 20, aged 58.

Schein, Herbert ⊕ Staten Island, N. Y.; Universität Köln (Cologne) Medizinische Fakultät, Köln, Prussia, Germany, 1925; member of the American Psychiatric Association; supervising psychiatrist, Willowbrook State School; died Jan. 30, aged 51, of cerebral thrombosis.

Schwartz, William D. ⊕ Portland, Ind.; Medical College of Indiana, Indianapolis, 1896; served as secretary of the Jay County Board of Health and as a member of the city school board; for many years president of the First National Bank, of which he was one of the organizers; affiliated with the Jay County Hospital, where he died Dec. 28, aged 82, of sarcoma.

Seibel, Ludwig J., Harvey, N. D.; University of Minnesota Medical School, Minneapolis, 1932; served on the staff of St. Aloisius Hospital; died Dec. 7, aged 60, of coronary disease.

Short, Zuber Nathaniel ⊕ Hot Springs National Park, Ark.; Hahnemann Medical College and Hospital of Philadelphia, 1895; fellow of the American College of Surgeons; on the staff of St. Joseph's Hospital; died Dec. 25, aged 79, of pneumonia.

Smith, Vine LaRue, Detroit; Saginaw Valley Medical College, Saginaw, Mich., 1898; died Dec. 24, aged 77, of coronary thrombosis.

Stevens, Neil Campbell, Walpole, N. H.; Columbia University College of Physicians and Surgeons, New York, 1915; died in Melbourne, Fla., Dec. 23, aged 63, of coronary occlusion.

Sutherland, William Leonard ⊕ Rexburg, Idaho; Rush Medical College, Chicago, 1915; county health officer; died Jan. 10, aged 63, of injuries due to a fall.

Watters, Phil Ganz ⊕ Des Moines, Iowa; University of Nebraska College of Medicine, Omaha, 1920; member of the American Academy of General Practice; died in Iowa Lutheran Hospital Dec. 12, aged 58, of cardiac decompensation and arteriosclerosis.

Westerfield, Aretus Allen, Utica, Ky.; Barnes Medical College, St. Louis, 1896; died Dec. 30, aged 80, of angina pectoris.

Whittle, Charlton Cash, Tucson, Ariz.; Jefferson Medical College of Philadelphia, 1911; formerly affiliated with Indian Service; died Nov. 4, aged 72.

Wier, Daniel Stuart ⊕ Beaumont, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1893; fellow of the American College of Surgeons; on the staff of the Hotel Dieu Hospital, where he died Jan. 15, aged 81, of bronchopneumonia.

Willison, Eugene Emerson ⊕ Merced, Calif.; Indiana University School of Medicine, Indianapolis, 1927; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; affiliated with Mercy Hospital and Merced General Hospital; died Jan. 24, aged 54, of heart disease.

Wills, Leonidas Edmund ⊕ Columbus, Ohio; Ohio Medical University, Columbus, 1897; died Dec. 11, aged 81.

Yates, Claud ⊕ Philadelphia, Miss.; Memphis (Tenn.) Hospital Medical College, 1912; formerly affiliated with Indian Service; died in Baptist Memorial Hospital, Memphis, Tenn., Jan. 19, aged 69.

Young, Carlie R., Angier, N. C.; University College of Medicine, Richmond, 1908; died Dec. 5, aged 71, of chronic bronchitis.

Young, Edward Milton ⊕ Sheridan, Ind.; Illinois Medical College, Chicago, 1906; served during World War I; member of the library board; died in the VA Hospital, Indianapolis, Jan. 17, aged 83.

Ziegler, William H., Philadelphia; Jefferson Medical College of Philadelphia, 1880; for many years member of the board of education; served as a police surgeon; died Jan. 23, aged 97, of myocardial failure.

FOREIGN LETTERS

CHILE

Congress on Hydatid Disease.—The fourth International Congress on Hydatid Disease was held in Santiago, Chile, Nov. 21-24, 1952. Dr. H. Dew of Australia read a paper on pleomorphism in hydatid disease. He described the morphology of the larval stage of this disease in the sheep, the ox, and in man. In the sheep, which is the ideal intermediate host, simple, multilocular, and multicystic varieties are common, while in the ox the commonest type is the multilocular. In man simple cysts and cysts containing daughter cysts are the commonest type, but another type is found in bones. In addition, alveolar hydatid disease and types combining this and other forms may occur. The controversy, now nearly a century old, concerning the nature of these latter forms has recently been reconsidered and the statement made that the monist doctrine must now be universally accepted: there is only one type of adult Taenia. These protean manifestations of the disease must be regarded as the larval forms of the same parasite and the essential unity of the hydatid species admitted. Dr. Dew referred to the early stages of development of the cyst in the experimental animal, the types of cellular reaction illustrated, and the evidence that these abnormal forms are a reversion back to an earlier type. It is emphasized that in all these forms there is the common factor of deficient hyalin production. It is suggested that possibly the pleomorphism exhibited by the disease in all hosts is due to this factor and that this aberration of hyalin production may be induced by passage through the ox rather than the sheep. At another time Dr. Dew referred to the hydatid of the brain and enumerated its most commonly recognized characteristics. It occurs most frequently in young subjects, usually takes the form of a simple univesicular cyst, and daugther cyst formation is rare. The adventitial capsule is poorly developed, sometimes being practically absent; erosion of the skull may occur, while clinically the disease is strangely latent. Dr. Dew then described a number of clinical cases and concluded that multiple primary cysts may occur and a careful investigation of the fields of vision and the use of other ancillary neurosurgical methods of examination are essential for accurate diagnosis. Air studies have both their uses and dangers. The Casoni test is relatively unreliable. Full exposure at operation, complete uncapping of the cyst, and complete evacuation of all hydatid material are essential for success.

Dr. Thomas B. Magath of the Mayo Clinic read a paper on the diagnostic tests for hydatid disease based on immunologic phenomena. He pointed out that hydatid disease causes immunologic responses by the host that are useful and important in the diagnosis of the disease. Perhaps the earliest of these responses studied was that of eosinophilia, which is now recognized to have little diagnostic value. Ghedini in 1906 first used the fixation of the complement as a diagnostic aid, and this was followed by the development of a precipitin test by Fleig and Lisbonne in 1907. Ascoli proposed the miostagmin test in 1910, and a year later Giani applied the Abderhalden reaction to patients with hydatid disease. A number of investigators used the cutaneous reactions, and Casoni published his results in 1912. The tests used most successfully and extensively are the complement fixation test and the intracutaneous test of Casoni. Various modifications of these tests have been proposed and used. The author discussed the tests he used for over 30 years. A number of attempts have been made to preserve the antigen over a long period of time. This has been important in the United States because cases of the disease occur infrequently and there is no steady source of reliable antigen. After many trials, it has been found that cyst fluid can be preserved indefinitely, either for complement fixation tests or for the Casoni test, with an aqueous solution of thimersol (merthiolate®) in a proportion of 1 to 50,000. Antigens preserved as long as 17 years have proved entirely satisfactory and are free from anticomplementary properties. Observations have also been made on the reaction of these two most frequently used tests to the viability of the hydatid cyst.

Dr. A. Neghme and associates read a paper on the conditioned hemolysis test in the diagnosis of hydatid disease. The authors utilized the conditioned hemolysis technique in the serum of 45 persons as a serologic diagnostic procedure in hydatid disease. They used the polysaccharide fraction of the hydatid cyst membrane as the antigen with which they sensitized sheep red blood cells. The serum was previously treated with sheep erythrocytes to eliminate the heterophil antibodies. The results obtained suggest that the reaction is highly specific; yet further experience is needed before any definite conclusions can be obtained. The medical, social, and economic implications of hydatid disease were also studied by Dr. A. Negme. For this purpose the problem was considered under two aspects: (1) hydatid disease in animals, and (2) hydatid disease in man. In 1951 the frequency of hydatid disease among cattle, sheep, and pigs was studied based on the information obtained from 44 slaughter houses in Chile. In the slaughtered animals, hydatid disease was found in 23% of cattle, 11.8% of sheep, and 19% of pigs. The loss that the confiscation of infested viscera means to the national economy approximates $11,500,000. The problem of hydatid disease in man and its economic implications are directly related with the rates of morbidity and mortality, the place of hospitalization, the temporary invalidism, and the suffering produced. The cost of hospitalization in the wards of the Beneficiencia Publica for persons suffering from hydatid disease during the last seven years is more than 15 million Chilean pesos. Finally, the authors made several considerations regarding the advantages of the prevention of the disease.

Health education in the prevention of hydatid disease was discussed by Dr. René Sotomayor. The author said that the problem of the educational control of hydatid disease should be treated specially through the elementary school and projected to the home and the community. This task can be carried out systematically, coordinating it with other health problems of the students and with preventive activities of several zoonoses in rural areas. He considered the need for preparing teachers to carry out such studies. Secondly he admits the necessity to organize the community so as to promote improved slaughter house sanitation, a decrease in the number of stray dogs, and the acknowledgment of social groups to their obligation to prevent Echinococcus infestation of dogs. The author also recommends the utilization of all means of public information and the usual propaganda techniques. Free treatment for dogs suffering from the disease should be available. The author stressed the necessity to direct the programs of adult antihydatid education toward the direct and active acknowledgment, both by individual persons and groups, that the cure of hydatid disease is very important.

Sylvatic echinococcosis and human hydatid infection in Canada was studied by Dr. M. Miller. He stated that vast areas in northern Canada are sparsely settled or uninhabited and support a rich fauna of wild herbivores and carnivores. The tapeworm Echinococcus granulosus is well established in carnivores, especially in the wolf, and the eggs are distributed over much of the area. They are ingested by wild herbivores, particularly the moose and the caribou, in which the hydatid cysts develop in the lungs. The completion of the cycle is assured when wolves, which prey naturally on moose and caribou, devour the infested animals. It is improbable that sylvatic echinococcosis presents a direct source of infection for humans. In recent years extensive x-ray surveys for tuberculosis made annually among the North American Indians and Eskimos have shown that pulmonary hydatidosis is not rare. Dogs, which are very numerous and highly prized by the native population, have

The items in these letters are contributed by regular correspondents in the various foreign countries.

shown 30% infestation. The natives depend, to a large extent, on the wild herbivores for food. In many areas herbivores are slaughtered in great numbers and the flesh used as human and dog food. In this manner the sylvatic cycle is broken into the domestic scene, and the natives, by infecting their dogs, initiate a cycle in their immediate environment in which they invariably play the role of intermediate host.

Hydatid disease in Australia was analyzed by Dr. Dew. He pointed out that the incidence in sheep has not declined and that in many areas it still reaches a figure of 50% in adult sheep. Similar figures were given for oxen. As these cysts are often sterile, this host is regarded as unimportant in the life cycle. Reference is made to the rarity of the disease in Western Australia, both in sheep and in man, and the appearance of a dingo-wallaby life cycle in parts of Queensland. Infestation in dogs may be as high as 50% in some areas, with an average of 20%. In man figures from all states except Tasmania show a very marked decline as compared with figures of 1925. It is pointed out that the southwestern part of Victoria still remains a hydatid area and that the public health authorities are aware of this. An increase in incidence in Tasmania has been commented on by many physicians of that state. The reasons given for the general decline in Australia are a better education in matters of hygiene, better standards of housing and living, and the effect of propaganda by the public health authorities and veterinarians. The methods of prophylaxis directed against infestation of the dog by strict slaughter house regulations and by special instructions to farmers and school education were discussed.

DENMARK

The Danish Cancer Register.—The Danish cancer register, formally inaugurated on May 5, 1942, is the first organization of its kind to cover the whole of the country in which it was established. It is a national body created by the Danish National Association for Combating Cancer. The register has received powerful support from the Danish public health authorities, the Danish Medical Association, and other bodies. During the first 10 years of its existence, under the guidance of Dr. Johannes Clemmesen of Copenhagen, the register has published some 30 reports in English and has also taken an active part in international health affairs.

The register has not been concerned with the study of the results of various methods of treatment. Its primary object has been to investigate, in Denmark and elsewhere, the incidence of the malignant diseases and their endemiology or epidemiology. Hospitals throughout Denmark cooperate on a voluntary basis in reporting to the register all cases of carcinoma, sarcoma, and various other diseases, including all the cases of tumor of the brain and bladder. These reports are drafted to provide every detail of possible interest, including, for example, special data when twins are concerned. The register also receives reports from pathological institutes where postmortem and histological examinations are made. Another source of information is death certificates, which are checked at the register for data concerning cancer patients who have not passed through any hospital.

In *Nordisk Medicin* for Dec. 19, 1952, Dr. Clemmesen draws attention to the contribution made by the register to the study of the influence of heredity on the incidence of cancer. While heredity apparently does not play a very important part in the genesis of cancer of the cervix uteri, it may have some influence on cancer of the corpus uteri and on cancer of the breast. It has also been found that cancer of the left breast occurs more frequently than that of the right breast, in the ratio of 111:100, and that close relatives of breast cancer patients are more likely to have breast cancer on the same than on the opposite side. The register has also revealed a remarkable rise in the mortality in Copenhagen from lung cancer in males. The rate has risen from 5 per 100,000 population in 1931 to 37 per 100,000 in 1950. In the same period the mortality from lung cancer in women rose from 4 to 5 per 100,000 population. The corresponding rise in Danish provincial towns was less marked and still less in rural districts.

Poliomyelitis in Copenhagen in 1952.—The metropolitan area of Copenhagen is served by a single hospital, the Blegdam Hospital for communicable diseases. Between July 24 and Dec. 3, 1952, as many as 2,722 patients with poliomyelitis, 866 with paralysis, were admitted to this hospital. In four months three times as many patients with respiratory insufficiency as had been encountered in the preceding 10 years were treated. As many as 70 patients required artificial respiration at the same time. Prof. H. C. A. Lassen, who is in charge of the hospital, has recently stated that this outbreak of poliomyelitis was of greater proportions than any ever recorded in Europe.

The great number of serious cases necessitated use of improvised therapy. The supply of respirators was wholly insufficient. Until the last week of August, the therapeutic measures employed from 1948 to 1950 were still in use, and the mortality rate for patients with respiratory paralysis was 85 to 90%. At this stage extensive use was made of early tracheotomy with insertion of a tightly fitting rubber cuff tube. This was combined with bag ventilation, repeated aspiration and bronchoscopy, postural drainage, and the use of a stomach tube. Professor Lassen points out in the London *Lancet* for Jan. 3, 1953, that this system has reduced the mortality of respiratory paralysis cases from over 80% to about 40%. He writes: "I do not think that this method is ideal. It certainly needs to be perfected, and we are working at improving it."

This, the so-called Copenhagen scheme, required a large amount of skilled assistance, which was generously supplied by medical students. During several weeks when 40 to 70 patients required continuous or intermittent bag ventilation, about 200 medical students assisted daily. Their pay was about 30 shillings for eight hours. The daily cost of the gas mixture per patient was approximately the same amount. Although the extensive employment of skilled human aid as a substitute for mechanical respirators was costly, in this situation, the supply of respirators was quite inadequate, allowing no alternative course of action.

Cancer of the Lungs.—Many recent articles in the literature have stressed the increasing frequency of lung cancer, usually bronchogenic carcinoma. Dr. Franz Heintzelmann, of the Frederiksberg Hospital, reports a study of 87 cases observed in the period 1946 to 1951. Classification of the patients according to age brought out the curious fact that it was the middle-aged rather than the aged who were most affected, for, within the narrow age limits of 55 to 64, there were as many as 35 patients, 32 of whom were men. Dr. Heintzelmann has concluded that operable cases of lung cancer are nearly always those that are asymptomatic when the disease is discovered more or less accidentally, for example, when mass radiological examinations for tuberculosis are made. This observation raises the question whether periodic mass examinations should be undertaken in search for cancer of the lungs. Such radiological examinations would be easily conducted and could be restricted to men of 40 to 60 years. Dr. Heintzelmann is skeptical, however, as to the effectiveness of such serial examinations, for bronchogenic carcinoma may progress so rapidly that prophylactic examinations would have to be repeated at very short intervals in order that the disease could be diagnosed in the operable stage.

In an editorial on cancer of the lungs that appeared in the organ of the Danish Medical Association, *Ugeskrift for Laeger*, for Dec. 4, 1952, the tendency of relatively young men to have this form of cancer is emphasized. "The rise in the frequency of the disease, observed in Denmark since 1930 among younger men, particularly the less well-to-do in Copenhagen, is now more fully demonstrated than anywhere else. . . ." It is predicted that eventually the incidence of lung cancer will exceed that of all other forms of cancer combined. Reference is made to the cancer conference held at Louvain in July, 1952, when the evidence in favor of incriminating tobacco smoking, particularly cigarette smoking, was examined and endorsed. The editorial intimates that it must be possible to reduce the present high lung cancer mortality to that of 1931 by appropriate measures. These should include investigation of the exact composition and properties of tobacco smoke.

ECUADOR

Gastroduodenal Ulcers.—Dr. Juan Francisco Orellana, professor of gastroenterology of the Faculty of Medicine, Universidad Central of Quito, reported observations on 2,737 patients who had had gastroduodenal ulcers for more than 10 years. Several patients had been observed since the appearance of the first clinical symptoms. The ulcer was located in the duodenal bulb in 1,870 cases (68%) and in the stomach in 667 cases (32%). The ulcer was located on the lesser curvature in all cases of gastric ulcer. Some niches were observed on the greater curvature on radiological examination, but in all such cases the lesion was malignant. Examination of the gastric juice revealed hyperchlorhydria in 58% of the cases, normal chlorhydria in 25%, and hypochlorhydria in 15%. These findings show that hyperchlorhydria is not a necessary antecedent of the ulcers but is rather a complication of the ulcer. Pain was the predominant or the only symptom in every patient. In less than half of the cases, pain was associated with some other symptom, such as pyrosis or dyspepsia. As an asymptomatic period begins in the cycle of the disease, the ulcer craters diminish in size as the symptoms abate and disappear when the asymptomatic period is established. After asymptomatic periods of from two to six months, the niche reappears on roentgenograms, together with the symptoms of a new symptomatic cycle. The asymptomatic period is shorter in gastric ulcer than in duodenal ulcer. The following considerations are pertinent with regard to malignancy of the ulcers: 1. Gastric ulcers located on the horizontal portion of the lesser curvature frequently become malignant. 2. It is reasonable to suspect malignancy when the crater does not become smaller during the period of symptomatic improvement. 3. If the lesion becomes larger during the period of symptomatic improvement instead of decreasing or disappearing, it is probably malignant.

The most frequent and serious complications are those that occur in duodenal ulcer. Hemorrhage, perforation, and obstruction are the most frequent complications. In the cases observed by the author, hemorrhage occurred in 27% of the cases of duodenal ulcer. An emergency operation was necessary in 9.5% of the cases. Perforation occurred more frequently in cases of penetrating ulcers of the duodenal bulb (5.4%) than in cases of penetrating ulcers of the stomach (1.1%). Duodenal ulcers often produce obstruction, which in some cases is reversible. It is caused by edema, which is the early stage of the development of the ulcer. The hemorrhages were not preceded by any particular symptoms. In the majority of the cases, perforation was manifested by very acute stab pain. Both complications followed overindulgence in food and alcohol in a large number of patients.

Gastric ulcers respond well to clinical treatment. In accordance with the character of the ulcers, 84% of the ulcers responded well to clinical treatment, whereas surgical treatment was necessary in 16% of the cases with ulcers of the "sclerofibrous" type. Ulcers for which surgical treatment is necessary have a high mortality. The mortality was 7% in patients with ulcers who had clinical treatment and 50.6% in those who had surgical treatment, especially for the control of profuse hemorrhages. The author found that gastroduodenal ulcer is extremely rare in Indians. These data agree with those in the literature. The factors that prevent gastroduodenal ulcers in Indians are unknown.

Complications of BCG Vaccination.—Dr. Olga Rojas of the Antituberculous League of Ecuador observed the results of BCG vaccination in 14,500 infants and children. The vaccines were given to newborn infants, other infants, children of school age, and adolescents up to the age of 15 years. Lymphadenitis occurred in 22 cases. The lesions varied from a small and spontaneously reversible simple infarction to acute lymphadenitis that progressed to caseation. Lymphadenitis secondary to vaccination occurred oftener in newborn infants than in children of other age groups. The complication occurred two or three months after the vaccination. In none of the 22 patients in whom the complications occurred did tuberculosis develop. Cultures prepared with material taken from the suppurated lymph nodes gave positive results for tubercle bacillus in two cases. The bacillus corresponded to nonvirulent typical strains of BCG. In all cases, the complication followed a favorable course. In the majority of the cases there was a spontaneous regression. In other cases antibiotics had to be administered, and in still others surgical treatment was necessary.

Tuberculosis, Pregnancy, and Delivery.—Dr. Oscar Paladines, head of the maternity hospital of the Antituberculous League of Ecuador, reported a study on the course of pregnancy and delivery in normal women as compared to the course in 100 women with tuberculosis. He concluded that there is no difference in the course of pregnancy and the puerperium of normal and tubercular women. The number of abortions, premature deliveries, and stillborn fetuses is the same in both groups. In tubercular women the dynamics of the uterus were stimulated slightly, but the clinical course of parturition and of the puerperium is the same as in normal women.

LONDON

Americans Aid in Train Wreck.—One of the world's worst train wrecks occurred at Harrow on Oct. 8, killing at least 112 persons and injuring many more. American Air Force physicians, nurses, and hospital orderlies from units all over London went to the station in answer to a general alarm signal circulated by Scotland Yard. They were under the command of Col. C. Coler, of Third Air Force Headquarters, Ruislip. They brought stretchers, medical equipment, blankets, and blood plasma. Special supplies of plasma were flown from Burtonwood, the American air base in Lancashire, and the American physicians went into the center of the wreckage. As the injured were taken to a platform, which had been converted into an emergency casualty station, nurses gave immediate blood transfusions. A British physician said, "Without the Americans I would not like to say how many of the injured would have died. They have done a marvelous job of work." Mr. Lennox-Boyd, congratulating Colonel Coler, said, "You made a most extraordinary effort, most prompt in every way, acting as a generous ally. We are all most grateful."

Blood Transfusion in Paraplegia.—J. J. Walsh calls attention to the physical condition of many paraplegic patients. As a result of the depletion of the body's protein reserve, due to infection of the urinary tract and pressure sores combined with poor appetite and consequent low food intake, they are suffering from malnutrition. To reverse this protein deficiency, he gives transfusions. Their number and frequency and the amount of blood given at each transfusion depend on the individual case, but, in general, the greater the area of ulceration and the more toxic the patient, the more frequently are transfusions required. In the routine treatment of a new patient with extensive bedsores 3 to 4 pt. (1.7 to 2.3 liters) of blood are given in the first few days, followed by a weekly transfusion of 1 to 2 pt. (0.6 to 1.1 liters), until such time as the patient's clinical condition shows that he has overcome the toxemia and until his blood count remains high.

One serious drawback was that in numerous patients, after a variable number of whole blood transfusions, undesirable reactions to subsequent transfusions developed, despite the fact that no incompatibility was demonstrable in vitro. Investigations were carried out with a view to overcoming the difficulty, and good results were achieved with transfusions of red blood cell suspensions in such cases. So far the percentage of reactions following the use of cell suspension is negligible and far below that found after transfusions with full blood.

New Remedy for Vaginal Discharge.—McKay Hart and Hutton Brown of Glasgow have been testing various substances in the treatment of nonspecific cervicitis and vaginal thrush. They say that the most difficult cases are those that present no gross organic lesion as a cause for the discharge and from whom no definite pathogen can be isolated. They have been referred to loosely as nonspecific cervicitis. Hitherto the best of the remedies has been gentian violet, but this has certain disadvantages. It stains hands, clothing, and bed linen, and sometimes causes severe irritation. They have now tried a new preparation contain-

ing a sulphonated derivative of fuchsonium and sodium biborate. At first it was applied by the clinician twice weekly in the form of a white cream to the cervix and vault of the vagina. Later, the cream was obtained in tubes with a patent plastic applicator. The patients, after careful instruction, applied the cream each night on retiring.

Of 80 patients treated for cervicitis, 70 had rapid relief of subjective symptoms, the pruritus and irritation disappearing after two applications. The discharge persisted far longer, but subsequently 61 patients were completely cured, the discharge and all associated symptoms disappearing. In the remaining nine patients who showed initial improvement, the discharge was greatly reduced and became white and odorless. The other 10 patients, who did not improve on two treatments a week, were cured by daily treatment, except in one case, which showed a Trichomonas infection. Sixty cases of vaginal thrush gave even better results. In all cases the disease was related to pregnancy, and every case was cured, all irritation disappearing with the cheesy discharge of monilial origin.

Voluntary Spirit.—In spite of the nationalization of the health services and the virtual disappearance of voluntary hospitals, King Edward's Hospital Fund, with a capital of between 17 million and 19 million pounds, fulfills the first condition for continuing existence, that of adaptation to changing circumstances. The fund has never been a mere agency for the distribution of largess, nor has it been concerned only with the need of hospitals for monetary assistance. The amenities for which it pays include radio sets, tennis courts, film projectors, divan beds, and the like. It also aims at ward improvements, better facilities for nursing staff, more convenient kitchen equipment, and training of hospital domestic workers. To hospitals and other institutions outside the National Health Service, the fund in 1951 contributed $33,600 in maintenance grants and $210,000 in capital. One timely activity has been the sponsoring of a number of homes for the aged sick. They are intended to provide the right living conditions for hospital patients who have reached a certain stage of convalescence from illness or accident, but are slow to recover, as old persons are inclined to be.

Other work includes the emergency bed service, the hospital administrator's staff college, the recruitment and care of nurses, and the advisory catering organization, all of which show that the partnership of the state with voluntary service in hospital administration is a courageous and imaginative experiment. Most of the fund's income is the yield from invested capital, but it is interesting to find that it still enjoys the confidence of testators. In 1951 the amount received in legacies was $590,800. If the day of large bequests to charities is drawing to a close, it is not only because of the cessation of charitable impulses in a welfare state but also because, shorn by death duties, estates are only a ghost of their former selves.

LUXEMBOURG

Congress of Alienists and Neurologists of French-Speaking Countries.—This congress, which every year attracts Frenchmen, Belgians, Swiss, as well as scientists from other nations, was held in Luxembourg under the chairmanship of Professor Barre. T. Kammerer of Strasbourg discussed "Psychiatric Knowledge Acquired by Study of Twins." The gemellary method is based essentially on the comparative study of respective concordances between monozygotic and dizygotic twins. When the ratio of concordance is observed to be greater in the first group, one may conclude that there is a predominance of hereditary factors.

A. Donnadieu of Bordeaux presented a report on means of assistance to tuberculous mental patients. On the occasion of this congress, the *Bulletin of the Society of Medical Sciences* issued a special number devoted to this branch of medical sciences. The following reports were included: Cossa on "Present Classification of Epilepsy," Philippides on "Cerebral Arteriography and Surgical Treatment of Refractory Lumbosciatic Pain," Mische on "Possibilities and Limits of Electroencephalography," and Noesen on "Pyroshock Therapy and Examination and Treatment of Delinquent Persons."

MEXICO

Campaign Against Tuberculosis.—The results of the National Campaign Against Tuberculosis, now 23 years old, can be summarized as follows: 1. By now the total number of hospital beds is 3,500, of which 1,600 are in Mexico City and 1,900 in the states. Every one of the main hospitals, two of which are in Mexico City, one in Guadalajara (second largest city of the country), and one near the Gulf of Mexico, has a capacity of 350 to 900 beds, much equipment such as laboratories and x-ray departments, and modern facilities including those for research and teaching purposes. In spite of such achievements, this aspect of the problem is still far from completion, as it has been predicted that 10,000 tuberculosis hospital beds are necessary.

2. There are 47 dispensaries, distributed all through Mexico. They work in cooperation with the hospitals. Most of them have special buildings and adequate equipment. One of their developments is the application of the antituberculosis vaccine (BCG), which has been very satisfactory. This can be illustrated by the fact that from February, 1949, until July, 1952, 150,000 children of Mexico City have been vaccinated; in a group of more than 4,000 with careful follow-up studies not a single case of tuberculosis has been registered.

3. For mass x-ray surveys the Abreu system has been adopted; in every case a 35 mm. x-ray plate (at a cost of 25 cents) is taken. The survey began in 1940, and by now 1,300,000 plates have been taken, with very good results; many nonclinical cases of tuberculosis have been detected.

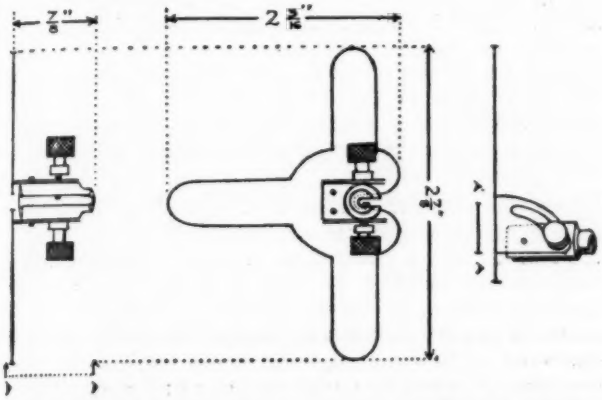
Last Works of President Alemán's Government.—In 1947 the government of President Alemán formulated a project of national works. Many of them were concluded or well advanced in the last quarter of 1952, that is in the final months of Alemán's stay in office. Among those related to teaching, or directly to medicine, that are already in practice or are supposed to be in 1953, the following can be mentioned: 1. Ciudad Universitaria (University City).—It is well known that the Universidad Nacional de México has up to now used a pattern similar to that of some of the old European universities in its distribution of buildings and offices; they are scattered in the oldest quarters of the city, without any direct connection between them. In this century, when the growing of Mexico City has been tremendous (present metropolitan population: 3,500,000), the situation has proved very inconvenient and a University City was planned to be built in the southern part of Mexico City, eight miles from downtown, in a site occupied until then by beds of volcanic lava. Work began in 1948, and now 70% of the total project, complete with offices, living quarters, sports facilities, and stadium, is finished. Among those units that will be finished next year is the building for the School of Medicine. 2. Ciudad Politécnica (Polytechnical City).—Planned for the Instituto Politécnico Nacional and with facilities similar to those of the Ciudad Universitaria, but smaller in magnitude and located in the northwestern part of the city, it is about 40% completed. 3. Hospitals.—During October and November, 1952, the Seguro Social (Government Department of Social Security) dedicated: (*a*) a hospital for workers and their families in the northern section of Mexico City. This hospital has 800 beds, outpatient departments, laboratory and x-ray units, and teaching and research facilities; (*b*) a hospital in the northern industrial city of Monterrey. Its capacity is 400 beds, and it has the same facilities as found in Mexico City; and (*c*) a hospital in Acapulco, planned for the study of tropical diseases.

The Department of Public Health and Social Assistance dedicated an Institute of Virology, in which particular emphasis will be put on poliomyelitis, which is a new disease in Mexico but which has spread out with great rapidity. Many other works of lesser importance were finished, including the Guardería Infantil of the Department of Communications and Public Works (an institution in which the workers of that department can leave their children during working hours). It is a very beautiful building, containing several works of art, and also having small medical units for the children under its care.

CORRESPONDENCE

MODIFICATION OF REYNOLDS NEEDLE HOLDER

To the Editor:—As a routine procedure we use intra-arterial injection for the administration of various drugs in the treatment of peripheral vascular diseases. The use of this method in such conditions as diabetic gangrene, acute and chronic ischemic syndromes of the lower limbs, and chronic lymphatic edemas is of the greatest value. We employ arterioclysis drop by drop (2 drops per diastole) of procaine (novocaine®) hydrochloride, 2-benzyl-2-imidazoline (priscoline®), or histamine. In gangrene accompanied by serious infection we use penicillin or oxytetracycline ("terramycin") added to the vehicle (almost always procaine) and vasodilators. Nevertheless, the motive of this communication is not to make a detailed study of this therapy but to report a modification effected by us in the needle holder of Reynolds.



On using the needle holder we had difficulty in puncturing the femoral artery through the orifice of the apparatus, which made the technique difficult. Thus we conceived the idea of converting this orifice into a channel (see figure), so that now we puncture the artery with the needle before collocation of the holder, and after the canalization of the artery is accomplished we fix our apparatus and proceed with the arterioclysis. On the other hand, we have shortened the needle holder barrel so that shorter needles may be employed. We have not found that this has caused any loss of stability. In conclusion, we believe that our modification makes the needle holder more practical and is thus worthy of note.

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CARE OF THE INDIGENT IN POLK COUNTY

To the Editor:—I would like to comment on the report under the Council on Medical Services (*J. A. M. A.* **151:**320 [Jan. 24] 1953) on medical care of the indigent in Polk County, Iowa, concerning an inaccuracy that I am certain represents a general misconception not only in Iowa but throughout the country. It was stated in the report that the county had no control over the quality of nursing homes. This is not completely true; for the city of Des Moines, which contains three-fourths of the population and 27 of the total 31 nursing homes in the county, has had a nursing home ordinance that within the past few months was recodified to include convalescent, rest, and keep and care homes with a definition of what constitutes a nursing home or convalescent home as well as a definition of a care and keep home.

Incidentally, the greater majority of physicians consider that any institution that cares for the aged, infirm, or chronically ill is a nursing home, which is definitely not true. Unfortunately, there are many such institutions that represent themselves as nursing homes and that have neither the facilities nor the personnel to render necessary care. The definition of a convalescent home and of care and keep homes, as given in the Des Moines ordinance, is as follows:

"a. *Nursing or Convalescent Home.* As used in this Ordinance, 'Nursing Home or Convalescent Home' is any institution, place, building or structure in which any accommodation is primarily maintained, furnished or offered for the care and board of two or more non-related invalid, infirm, aged convalescent or physically disabled persons requiring or receiving general nursing service and chronic or convalescent care including the administration of drugs and medicines.

"b. *Rest Home and Care and Keep Home.* As used in this Ordinance, 'Rest Home' and 'Care and Keep Home' is any institution, place, building or structure in which any accommodation is primarily maintained, furnished or offered for the care and board of two or more non-related invalid, infirm, aged or physically disabled persons requiring or receiving room and board and other services exclusive of general nursing, convalescent care and the administration of drugs or medicines."

There is a definite difference in our requirements for personnel, facilities, and equipment; we investigate the quality of care and periodically inspect. Actually, our licensed nursing homes are excellent institutions; however, the rest and care and keep homes that are now under the purview of the new ordinance are in dire need of control. A major feature of the new regulation is the placing of patients requiring nursing care in licensed nursing homes and not in any institution that gives some sort of care for the least amount of money.

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Director, Des Moines and Polk
County Health Departments
Des Moines, Iowa

The report of the Council on Medical Service was prepared before the recent recodification of the ordinance. This new information will be included in the Council's reprints, which are obtainable from the Council office.—Ed.

REGISTRATION OF PHYSICIANS FOR SERVICE

To the Editor:—The Medical Veterans Society is receiving numerous complaints that physicians are violating public law 779 (the "Doctor Draft act") by failing to register, either through ignorance of their responsibilities or through deliberate misrepresentation. Registration under public law 779 is required of every physician from the day he graduates up to his 50th birthday, unless he is a member of a reserve component. A commission in the Army of the United States does not automatically confer reserve status. It should be noted that the basic Selective Service Act prescribes severe penalties for failure to register or other violations of the law.

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VISITORS TO GREAT BRITAIN

To the Editor:—I visited your great country in 1939 and met many fellow physicians in places as far apart as New York and San Francisco. Owing to the war I have lost touch with all of them, but I still have many happy and stimulating memories of my visit. This year being coronation year, no doubt many of your readers will be visiting this country. With your permission, my wife and I would like to extend through your columns a warm welcome to American doctors visiting this beautiful part of our country. If any of your readers are interested and will write to the address below, we will do our best to accommodate them.

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Nr. Stourbridge, Worcs., England.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Medical Practice Acts: Reasonableness of Board's Rules.—The plaintiff filed a petition for a writ of mandamus to compel the defendant to issue plaintiff a license to practice medicine without examination. From a judgment granting the writ, the defendant appealed to the appellate court of Illinois, first district.

The plaintiff, a graduate of the University of Heidelberg, Germany, alleged facts, which were substantially admitted by the defendant, that indicated that the plaintiff had complied with the reciprocity provisions of the Illinois medical practice act. The defendant alleged, however, that the petitioner on seven different occasions voluntarily took written medical examinations and failed to receive a satisfactory grade in each of them and also alleged that there is a rule of long standing relating to the administration of medical practice that provides that an applicant who has failed in the written examination before the department is not permitted to apply for a license at a later date under the reciprocity provisions of the medical practice act. The defendant's sole contention, therefore, was that the department of registration and education in the exercise of its discretion was warranted in denying the license to the plaintiff because he failed in the medical examinations.

We assume, said the court, that the department did adopt and promulgate a regulation, as stated in the defendant's answer, although the plaintiff has challenged the existence of such a regulation. Section 7 of the medical practice act permits the department to prescribe rules and regulations for all examinations. Our courts have repeatedly held that the rules of the department may be reviewed to determine whether they are fair, reasonable, and impartial. As we read the pleadings, the court continued, the defendant admits that the plaintiff has complied with all the conditions prescribed by the medical practice act but insists that the plaintiff is barred from obtaining a license because he voluntarily submitted to examinations and failed to secure a passing grade. Under the circumstances shown by the pleadings, the court said, it would seem to us that application of the regulation relied on by the defendants imposes additional conditions on the plaintiff not provided for in the law. In our opinion, the court concluded, the regulation of the department is therefore unreasonable. Having once fully complied with the requirements of the act, the plaintiff is entitled to a license. The judgment in favor of the plaintiff requiring the department of registration to issue the plaintiff a reciprocity license without examination was therefore affirmed. *People ex rel. Schoenbaum v. Department of Registration & Education of State et al., 104 N. E. (2d) 662 (Illinois 1952).*

Admissibility in Evidence of Chemical Tests for Intoxication.—The defendant was charged with feloniously driving an automobile while under the influence of intoxicating liquor, and, from a judgment of conviction, he appealed to the district court of appeal, second district, division 1, California.

The defendant, following an accident in which his automobile was involved, was taken to the Tweedy Industrial Hospital. Dr. Makita, who operated the hospital, testified that when the defendant arrived "he was complaining of pain in the left elbow, pain in the chest, principally; and his breath was markedly alcoholic. . . . His temperature and respiration were normal, and he had a pulse rate of 80 and blood pressure of 120 over 75; and he was conscious and apparently not in shock." There was other testimony to the effect that the defendant's breath was alcoholic. The defendant, who had been conveying two other men on a drinking tour, denied having had anything to drink except two bottles of beer earlier in the evening. According to Dr. Makita's testimony, after treating the defendant's injuries, the defendant was asked "whether it was all right to draw blood for blood alcohol tests for the California Highway Patrol," and "he said it was all right. Put his arm out." Dr. Makita then "put a tourniquet around his arm and cleansed the area with benzine, and Dr. Kern . . . extracted the blood with a syringe." The sample so obtained was delivered to the California Highway Patrol, and a chemical examination disclosed that defendant's blood contained 0.21% of alcohol by weight. The defendant said that the blood extraction occurred while he was unconscious and without consent being given therefor. He claimed to have been unconscious from the time of the accident until waking up in the General Hospital between 9:00 and 10:00 the next morning and denied any recollection of being at the Tweedy Industrial Hospital.

Before trial, the defendant "moved the trial court to suppress evidence of the blood specimens coercively extracted from his body without his consent and the alcoholic tests of said samples." The grounds of this motion were that the use of said blood and any chemical analysis thereof in evidence would violate defendant's rights to due process of law and against self-incrimination and to not be a witness against himself and to not be compelled to furnish evidence against himself as guaranteed by the United States and California constitutions. The motion was denied, and the taking of this blood sample, its chemical analysis, and use in evidence, resulting in conviction, was the defendant's chief ground for reversal.

Cited and discussed in some detail by both parties, said the court of appeal, was the case of *People v. Rochin, 225 P. (2d) 1; 72 S. Ct. 205,* a prosecution for unlawful possession of a preparation of morphine. Two capsules containing the preparation were found by officers who broke into the defendant's bedroom without a warrant; later, the capsules, which had been swallowed by the defendant, were forcibly recovered by means of a stomach pump. The Supreme Court of the United States unanimously held that the conviction should be reversed on the ground that the conviction violated the due process clause of the Fourteenth Amendment in that the methods employed offended "a sense of Justice" and on the ground that the prohibition of self-incrimination in the Fifth Amendment imposed restraints not only on the federal government but also on the states.

An important difference between the Rochin case and the present prosecution is at once apparent, said the California court of appeal. In the Rochin case there appears to be no doubt that the morphine capsules were illegally obtained. Three deputy sheriffs broke into the defendant's room, "jumped upon the defendant, grabbed him by the throat," in an unsuccessful effort to recover the capsules that defendant had swallowed; defendant was then handcuffed, taken to a hospital, strapped on an operating table, and the capsules containing morphine were forcibly retrieved by the use of a stomach pump. In the instant case, however, continued the court, the record discloses no such aggravated situation but merely presents a direct conflict on the question whether the blood sample was taken with or without the defendant's consent. Obviously if consent was given, any apparent similarity between the two cases ceases to exist. The testimony of Dr. Makita, who attended the defendant at the Tweedy Industrial Hospital, has already been referred to and furnishes substantial evidence that consent was given, notwithstanding the defendant's denial thereof. It was likewise Dr. Makita's testimony that the defendant was then conscious, moving around, and uncooperative; "he wanted to smoke and wanted to drink, and this and that."

A review of the record, concluded the court, shows that the defendant was accorded a fair and impartial trial and that the judgment of conviction was supported by substantial evidence. Accordingly, the court of appeal held that the trial court's refusal to suppress evidence of the blood test was proper, and the judgment of conviction was therefor affirmed. *People v. Frederick, 241 P. (2d) 1039 (California 1952).*

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Ind. Hyg. & Occupat. Medicine, Chicago

6:469-558 (Dec.) 1952

INDUSTRIAL HEALTH EXPERIENCES IN PENNSYLVANIA

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Union Health Center Fosters Employee Health: Philadelphia Experience. J. A. Langbord.—p. 474.
Pittsburgh Experience in Undergraduate and Graduate Industrial Medical Education. T. L. Hazlett.—p. 476.
Industrial Medical Association and Medical Directors' Club in Pittsburgh. D. C. Braun.—p. 477.
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Chemical Alopecia: Unique Case. G. E. Morris.—p. 530.

A.M.A. Arch. Neurology and Psychiatry, Chicago

69:1-144 (Jan.) 1953

*Mesencephalotomy in Treatment of "Intractable" Facial Pain. E. A. Spiegel and H. T. Wycis.—p. 1.
Language Behavior in Manic Patients: Qualitative Study. M. Lorenz.—p. 14.
Incisural Sclerosis and Temporal Lobe Seizures Produced by Hippocampal Herniation at Birth. K. M. Earle, M. Baldwin and W. Penfield.—p. 27.
Problems in Supervision of Psychiatric Residents in Psychotherapy. M. Rosenbaum.—p. 43.
Infectious Mononucleosis with Diffuse Involvement of Nervous System: Report of Case. M. J. Freedman, L. T. Odland and E. A. Cleve.—p. 49.
Diagnostic and Therapeutic Clues in Study of Tetanus. R. P. Schmidt, L. L. Levy, R. C. Turreli and others.—p. 55.
Familial Ocular Myopathy and External Ophthalmoplegia. R. S. Beckett and M. G. Netsky.—p. 64.
*Epilepsia Cursiva: Syndrome of Running Fits. G. C. Sisler, L. L. Levy and E. Roseman.—p. 73.
Prolonged Posteclamptic Aphasia: Report of Case. M. L. Simmel and K. H. Goldschmidt.—p. 80.
Effect of Dimercaprol (BAL) in Hepatolenticular Degeneration: Report of Case, with Clinical and Electroencephalographic Study. M. Streifler and S. Feldman.—p. 84.
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Histamine Therapy in Acute Ischemia of Brain: Report of 50 New Cases. A. R. Furmanski.—p. 104.
Problems Related to Treatment of Intracranial Aneurysms by Carotid Ligation. R. R. J. Strobos and L. A. Mount.—p. 118.
Reluctance to Move Paretic Muscles. R. M. Brickner.—p. 129.

Mesencephalotomy in Treatment of Intractable Facial Pain.—Facial pain that persists not only after the usual conservative therapeutic methods but also after neurosurgical procedures is a challenging problem. Spiegel and Wycis describe six cases of this type in which they produced electrolytic lesions in the pain-conducting pathways at the mesencephalic level by means of the stereoencephalotome (mesencephalotomy). In three cases in which the diagnosis was tic douloureux, retrogasserian rhizotomy had previously been performed by neurosurgeons; in a fourth case thalamic pain had been refractory also to cortical operations; and in a fifth case pain of pontine origin had persisted after contralateral prefrontal lobotomy. In the first three cases lesions were produced in the dorsomedial nuclei of the thalamus (mesencephalothalamotomy) as well as in the mesencephalon in order to reduce the emotional reactions accompanying possible remaining pain perception. In the cases with organic thalamic and pontine lesions mesencephalotomy alone was performed. One patient had been free of pain for four and one half years at the time of writing and the other for nine months. Transitory relapse occurred in one case after more than three years. In two other cases the postoperative period had been too short to permit definite appraisal. The thalamic pain in one case was relieved for only four and one half months, probably owing to the incomplete interruption of the pain-conducting system; this case illustrates the important part played by afferent impulses in the pathogenesis of thalamic pain.

Running Fits (Epilepsia Cursiva).—Sisler and associates define a running fit as an episodic alteration of awareness associated with running. Consciousness may be clouded to a variable degree. The activity is inappropriate to the reality situation, that is, the running fit is a type of automatism and the syndrome is included in the ill-defined group of psychomotor epilepsies. The authors describe observations on nine patients ranging in age from 7 to 26 years. Five were females and four were males. The ages at the time of onset of the running fits varied between 5 and 24 years. All had in addition to the running fits grand mal and/or psychomotor seizures. Dysrhythmic electroencephalograms with temporal spikes were also observed in all cases. The patients were of heterogeneous personality types, and many had conflicts in relation to members of their families. The histories suggest that these conflicts acted as precipitating factors in the illness and that the running was an expression of the conflict. Phenobarbital and diphenylhydantoin medication was used, combined with superficial psychotherapy of a reassuring and explanatory type. In almost all cases this treatment produced seizure control and decrease in behavior problems. The condition described is known also as epilepsia cursiva, but although this term is found in medical dictionaries, it is rarely used in the literature. Running fits have been observed in dogs fed flour treated with nitrogen trichloride (agene®). Ingestion of this type of flour by human subjects has never been known to produce running fits.

A.M.A. Arch. Ophthalmology, Chicago

49:1-116 (Jan.) 1953

Goniotomy for Glaucoma Associated with Aniridia. O. Barkan.—p. 1.
Osteogenesis Imperfecta Congenita and Blue Sclerotics: Clinicopathologic Study. A. D. Ruedemann Jr.—p. 6.
Beta-Radiation Therapy of Pterygium. J. W. Rosenthal.—p. 17.
Evaluation of Five New Cycloplegic Drugs. B. C. Gettes and I. H. Leopold.—p. 24.
Normal and Reversed Vision in Transplanted Eyes. L. S. Stone.—p. 28.
*Idiopathic Detachment of Retina: Analysis of Results. T. R. Smith and L. H. Pierce.—p. 36.
Blepharoptosis Treated by Friedenwald-Guyton Suture. B. Smith and H. G. Pang.—p. 45.
Surgical Aspects of Defective Abduction. E. B. Spaeth.—p. 49.
Electroretinogram: Review of Literature. G. W. Bounds Jr.—p. 63.
Lids, Lacrimal Apparatus, and Conjunctiva: Review of Recent Literature. J. H. Allen.—p. 90.

Idiopathic Detachment of Retina.—The histories of 618 patients with idiopathic detachment of the retina examined and treated at the Massachusetts Eye and Ear Infirmary between 1947 and July, 1951, are reviewed. Operations were performed in 525 cases either by attending physicians, by physicians of the retina service, or by the resident staff. Operation was successful in 70% of the cases. When follow-up observation is continued,

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Titles marked with an asterisk (*) are abstracted.

this figure may be raised to 74%. The prognosis for retinal reattachment was poorer when there was (1) detachment of the macula; (2) fixed folds of the retina; (3) total detachment of the retina; (4) no break or two or more breaks; or (5) aphakia with fixed folds. Variations in the methods used to treat the breaks and to release subretinal fluid could not be demonstrated to affect the therapeutic result. However, the prognosis was better when it was not necessary to release subretinal fluid. Preoperative hemorrhage occurred in at least 10% of the cases. The retina in the fellow eye was detached in 27% of the cases. Myopic patients tend to have detachment of the retina at an earlier age than patients with other refractive errors.

A.M.A. Arch. Pathology, Chicago

54:507-592 (Dec.) 1952

Osteoma, Ossifying Fibroma, and Fibrous Dysplasia of Facial and Cranial Bones. A. G. Smith and A. Zavaleta.—p. 507.
Hyaline Material with Staining Reaction of Fibrinoid in Renal Lesions in Diabetes Mellitus. L. G. Koss.—p. 528.
Vitamin A. Deficiency in Duck: Skeletal Growth and Central Nervous System. S. B. Wolbach and D. M. Hegsted.—p. 548.
Peliosis Hepatis: Report of Three Cases, with Discussion of Pathogenesis. F. T. Hamilton and J. M. Lubitz.—p. 564.
Arteriosclerosis in Dog: II. Aortic, Cardiac, and Other Vascular Lesions in Thyroidectomized-Hypophysectomized Dogs. S. Lindsay, H. Feinberg, I. L. Chaikoff and others.—p. 573.

Alabama State Medical Assn. Journal, Montgomery

22:147-170 (Dec.) 1952

Asterol Treatment of Superficial Fungus Infections. H. W. Slaughter.—p. 147.
Current Treatment of Tuberculosis. A. J. Viehman.—p. 150.
Respiratory Urography. A. L. Atwood.—p. 153.
Total Pelvic Evisceration: Report of Four Cases. H. S. J. Walker Jr.—p. 154.

American Journal of Clinical Pathology, Baltimore

23:1-100 (Jan.) 1953

What's Past is Prologue. I. Davidsohn.—p. 1.
*Reproducibility and Constancy of Platelet Count. G. Brecher, M. Schneiderman and E. P. Cronkite.—p. 15.
*Newer Methods of Detection of Incompatibilities in Blood Transfusion. O. B. Hunter Jr. and J. B. Ross.—p. 27.
Clinical Value of Serum Thyroxine Determination. V. E. Chesky, W. C. Dreese, B. O. Duboczky and others.—p. 41.
Evaluation of Iodoacetate Test for Cancer. J. Lebowich.—p. 45.
Plasma Levels of Viomycin in Man After Single Intramuscular Injection. W. E. Dye and W. F. Bull.—p. 56.
Review on Flame Analysis in Clinical Laboratory. B. Zak, R. E. Mosher and A. J. Boyle.—p. 60.

Constancy of Platelet Count.—Capillary and venous platelet counts were performed on 13 healthy men. Eight counts were performed on one sample of venous blood and eight counts on successive drops of capillary blood on each of four different dates. The four series were spaced four to six weeks apart over a five month period. Results showed that direct platelet counts performed with the phase microscope on venous blood collected in siliconed test tubes accurately reflect the circulating platelet level. The error of the single count is 11%, and can be reduced only by multiple counts. Platelet counts on capillary blood from a finger puncture are subject to greater errors (24%), and the counts are on the average 2½% lower. This is presumably due to a variable loss of platelets in the puncture wound and does not necessarily indicate a lower circulating capillary platelet level. The main advantage of the platelet counts with the phase microscope is the easy and certain recognition of individual platelets, and it is believed that this accounts for its satisfactory reproducibility, even by inexperienced technicians. Other methods of platelet counting are reviewed, and the necessity for detailed statistical analysis of counts is illustrated. In this study platelet levels varied greatly among individuals, but in each man the count showed only minor variations during a five month period.

Incompatibilities in Blood Transfusion.—Since June, 1950, five methods have been used routinely by the authors for the detection and identification of incompatibilities in blood transfusion. In order of increasing sensitivity these are the saline tube test, slide test, albumin tube test, indirect Coombs' test, and trypsin-treated red cell test. The last two tests proved to be the most sensitive for the detection of red cell antibodies in serum of 1,400 obstetrical patients and recipients of blood transfusions. Of the 1,400 serums tested, 217 contained Rh antibodies demonstrable by the most sensitive techniques. It was believed that 100% of antibodies were detected by the trypsin-treated red cell test. The different characteristics of antibodies and the relative incidence of their respective antigens in the population are helpful in determining the specific type of antibody causing transfusion reactions. The modified protein tube test is the most efficient for doing routine transfusion cross matching. Most significant antibodies will be detected by the standard cross-matching technique as follows: A 2% suspension of donor's cells in donor's serum or 6% albumin is prepared. To two drops of patient's serum, one drop of donor's cell suspension is added. A clean Kahn tube is used for the test and placed in a water bath at 37 C for a minimum of 30 minutes. After removal from the water bath centrifugation is carried out at 1,500 rpm. for one minute. After removal from the centrifuge packed cells are carefully observed by gentle shaking for clumping of red cells. In case of doubt, a drop of cell suspension is placed on a slide and observed through the microscope.

American Journal of Ophthalmology, Chicago

35:1737-1874 (Dec.) 1952

Experimental Herpes Simplex. A. E. Braley.—p. 1737.
*Relationship of Retinal and Renal Arteriosclerosis in Living Patients with Essential Hypertension. J. P. Wendland.—p. 1748.
*On Character and Management of Circulatory Disturbances of Central Retina. J. V. V. Nicholls.—p. 1753.
Use of Hyaluronidase in Ophthalmology. F. R. Carriker.—p. 1765.
Central Angiospastic Retinopathy: Review of Literature and Report of One Case. R. Buxeda.—p. 1769.
Method of Lower Lid Reconstruction. S. D. McPherson Jr.—p. 1775.
Ocular Findings in Gout: Report of Case of Conjunctival Tophi. J. R. McWilliams.—p. 1778.
Effect of Intravenous Typhoid Vaccine on Adrenal Cortex Function. D. A. Rosen.—p. 1783.
Diagnosis of Ocular Tumors of Various Types. E. B. Spaeth.—p. 1791.
Annular Malignant Melanoma of Iris and Ciliary Body: Report of Case and Summary of Literature. P. A. Rockwell.—p. 1806.
Topical Therapy in Inclusion Conjunctivitis. H. L. Ormsby, G. A. Thompson, G. G. Cousineau and others.—p. 1811.
Transient Abolition of Pupillary Reaction to Convergence in Presence of Intact Convergence and Accommodation and Normal Pupillary Reaction to Accommodation in Case of Tumor of Pineal Gland. W. Kornblueth.—p. 1815.

Relationship of Retinal and Renal Arteriosclerosis.—The degree of sclerosis of the retinal and renal arterioles was determined in 80 patients with essential hypertension severe enough (average blood pressure 206/127 mm. Hg) to require sympathectomy. The retinal arterioles were evaluated by fundoscopic examination and the kidney arterioles by biopsy at the time of sympathectomy. The severity of the arteriolosclerotic process in both regions was graded on the same scale of zero through four grades. In 69 (86%) of these patients the eyes and kidneys either showed the same degree of sclerosis or the difference was not more than one grade. When there was a difference, the greater change was found oftenest in the retina. A total of 23 of the patients showed no renal arteriolosclerosis, but when it is considered that 19 of these 23 already had hypertension of sufficient severity and duration to have organic changes in their retinal arterioles, it seems unwise to conclude, as Goldblatt does, that renal arteriolosclerosis is the usual cause of essential hypertension. The results in the present investigation are much more in accord with the view that the arteriolosclerosis in the kidney is either the direct result of the hypertension or an independent process enhanced by the hypertension. Comparing the frequency of retinal arteriolosclerosis in glomerulonephritis with that in essential hypertension, Wendland says that Graham found that only 8 of 39 patients with glomerulonephritis proved by necropsy and hypertension had retinal arteriolosclerosis, whereas in his 80 patients with essential hypertension all but four showed some degree of retinal arteriolosclerosis. Hypertension often develops terminally in glomerulonephritis; this seems to corroborate the common belief that at least one of the factors that determine the extent

of the sclerosis of the retinal arterioles is the duration of the hypertension. Patients with glomerulonephritis and hypertension do not live long enough to develop retinal arteriolosclerosis.

Circulatory Disturbances of Retina.—Nicholls presents the histories of 23 consecutive patients with circulatory disturbances in the central retina. No selection was made, save to exclude patients with malignant hypertension, nephritis, or diabetes mellitus. The cases are arranged in diagnostic groups. The first three cases represent central choroidal sclerosis. There was little or no change in the retinal vessels, and the condition appeared to be due entirely to sclerosis of the choroidal vessels. The fourth case was one of Tay's central choroiditis. In case 5 a mixture of choroidal sclerosis and retinal circulatory changes was suggested. In cases 6, 7 and 8 the diagnosis was circinate retinitis. The next four patients had typical examples of senile macular degeneration. The next five patients had essentially the same condition, but all of these patients had mild to moderate hypertension. The last six patients had what might be classified broadly as central angiospastic retinopathy. The ophthalmoscopic appearance and pathogenesis of these conditions can be accounted for on the basis of the interplay of four factors: arteriolar spasm and arteriolar sclerosis that affect the choroidal and retinal circulations either separately or together. The present study indicates that these conditions, though traditionally considered entities, actually overlap and form a group. Emotional stress plays an important etiological role. Contrary to the traditional view, therapy is helpful. This should be rational and directed to reduction of the emotional stress and to producing vasodilatation. Treatment was most effective and the prognosis best in patients who were younger, whose disease was of shorter duration, and in whom arteriolar sclerosis was less pronounced and angiospasm associated with anxiety was the most prominent feature.

American Journal of Physical Medicine, Baltimore

31:415-478 (Dec.) 1952

Management and Treatment of Manic-Depressive Syndrome in an Occupational Therapy Clinic. B. S. Condon.—p. 415.
Influence of Microwave Irradiation on Bone Temperature in Dog and Man. B. K. Hutt, J. Moore, P. C. Colonna and S. M. Horvath.—p. 422.
Function of Serratus Anterior: Clinical Study of Chest Surgical Patients. H. B. Doppelt.—p. 429.
Degeneration of Lumbar Intervertebral Discs. E. Hasner, H. H. Jacobsen, M. Schalimtzek and others.—p. 441.
Cortisone in Treatment of Rheumatoid Arthritis. E. S. Gordon.—p. 451.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

68:875-1046 (Dec.) 1952

Chondroectodermal Dysplasia (Ellis-Van Creveld Disease): Report of Three Cases. J. Caffey.—p. 875.
Roentgen Appearance of Small Intestine in Tuberculous Peritonitis Before and After Streptomycin Therapy. J. T. Brackin Jr., J. M. Miller and W. H. Bell.—p. 887.
Roentgen Demonstration and Significance of Pedicle in Polypoid Tumors of Alimentary Tract. B. R. Young and R. L. Scanlan.—p. 894.
Cholecystography: Comparison Study of New Cholecystographic Medium and Priodax in 50 Patients. I. R. Berger, J. W. Gaddis and E. L. Pirkey.—p. 900.
Intravenous Urographic Contrast Media: Controlled Study of Diodrast and Neo-Iopax. W. H. Mullen Jr. and C. R. Hughes.—p. 903.
Neo-Iopax: Relationship Between Degree of Reactions and Time of Intravenous Injection. J. L. Armbruster and H. W. Hefke.—p. 915.
Calcinosis in Scleroderma. M. D. Ingram Jr.—p. 918.
Centers of Ossification of Skeleton. B. R. Girdany and R. Golden.—p. 992.
Clinical Results Following Different Methods of Radium Application Used in Treatment of Cervical Cancer from 1921 to 1947. M. Bonebrake, A. I. Sherman, M. Ter-Pogossian and A. N. Arneson.—p. 925.
Physical Approach to Design of Applicators in Radium Therapy of Cancer of Cervix Uteri. G. H. Fletcher, R. J. Shalek, J. A. Wall and F. G. Bloedorn.—p. 935.
Non-Uniform Filter to Produce Flat Isodose Surface of Roentgen-Ray Intensity. M. A. Greenfield and K. Hand.—p. 950.
Steroid Hormone Therapy in Mammary Carcinoma. I. Macdonald, F. E. Davis and G. Jacobson.—p. 954.
Method Using I^{131} for Determination of Abnormal Thyroid Morphology. W. E. Goodwin, F. K. Bauer, T. F. Barrett and B. Cassen.—p. 963.

American Review of Tuberculosis, New York

67:1-122 (Jan.) 1953

Extrapleural Pneumothorax. J. W. Strieder and E. A. Gaensler.—p. 3.
Intermediary Report of 102 Streptomycin-Protected Pulmonary Resections. J. D. Murphy and B. B. Becker.—p. 22.
Bronchiectasis: Comparative Study. J. Gordon and P. C. Pratt.—p. 29.
*Transient Undiagnosed Intrathoracic Lymphadenopathy in Apparently Healthy Persons. A. D. Chaves and H. Abeles.—p. 45.
Cytology of Tubercle Bacillus with Reference to Mitochondria and Nuclei. L. C. Winterscheid and S. Mudd.—p. 59.
Tuberculosis Control in Hospital Personnel: Review. H. M. Riggins.—p. 74.
Tuberculosis Among Jews: Mortality and Morbidity Among Different Jewish Ethnic Groups. Tuberculosis Among Yemenite Jews. Etiologic Factors. J. Rakower.—p. 85.
Horner's Syndrome Complicating Surgery for Pulmonary Tuberculosis: Review of Five Cases. E. J. Welch.—p. 94.

Transient Intrathoracic Lymphadenopathy.—In 12 asymptomatic men and 8 asymptomatic women, survey chest roentgenograms revealed the presence of obvious enlargement of intrathoracic hilar lymph nodes of an indeterminate nature that subsequently underwent spontaneous regression. With the exception of one 52-year-old woman, all the other patients were between the ages of 19 and 31. Of the 20 patients, 15 were white and 5 were Negro. Ten patients had negative cutaneous reactions to 1 mg. of old tuberculin. Eighteen patients had bilateral and two had unilateral involvement. Enlargement of peritracheal lymph nodes occurred in seven patients. In only 11 patients were serial roentgenograms made often enough to indicate the rate of regression of the lymphadenopathy; complete disappearance of the lymphatic enlargement was observed within two and one-half to nine months. All of the patients, observed for a mean period of five years, have remained in good health without evidence of recurrence or other visceral involvement. It is emphasized that there is no implication that the findings in these patients with unexplained silent enlargement of intrathoracic lymph nodes represent a distinct disease entity or that intrathoracic lymphadenopathy per se is a trivial finding that does not require serious diagnostic measures.

Annals of Internal Medicine, Lancaster, Pa.

37:1123-1338 (Dec.) 1952

*Hyperthyroidism—An Evaluation of Treatment with Antithyroid Drugs Followed by Subtotal Thyroidectomy. E. C. Bartels.—p. 1123.
*Disturbance of Normal Bacterial Ecology by Administration of Antibiotics with Development of New Clinical Syndromes. D. T. Smith.—p. 1135.
New Drug Therapies in Arterial Hypertension. R. W. Wilkins.—p. 1144.
Incidence and Etiologic Background of Chronic Biologic False-Positive Reactions in Serologic Tests for Syphilis: Preliminary Report. J. E. Moore and C. F. Mohr.—p. 1156.
Ratio Between Phospholipid and the Cholesterols in Plasma as an Index of Human Atherosclerosis. R. S. Jackson and C. F. Wilkinson Jr.—p. 1162.
Diet and Atherosclerosis. L. M. Morrison.—p. 1172.
Basic Principles in Therapy of Diabetes. H. T. Ricketts.—p. 1181.
Diabetic Coma—A Therapeutic Problem. G. G. Duncan.—p. 1188.
Acute Respiratory Failure in Multiple Sclerosis and Its Management. T. C. Guthrie, J. F. Kurtzke and L. Berlin.—p. 1197.
Amyotrophic Lateral Sclerosis on Guam: Clinical Study and Review of Literature. D. R. Koerner.—p. 1204.
Alcohol-Oxygen Vapor Therapy of Pulmonary Edema: Results in 50 Attacks. M. A. Goldmann and A. A. Luisada.—p. 1221.
Life Stress, Emotions and Painful Stiff Shoulder. T. H. Lorenz and M. J. Musser.—p. 1232.

Treatment of Hyperthyroidism.—In the past eight and one-half years 2,400 patients with hyperthyroidism have been given one of the antithyroid drugs until a euthyroid state was established and then treated by radical subtotal thyroidectomy. Of these 2,400 patients, 1,500 received propylthiouracil in doses of 200 to 400 mg. daily, and 214 were given methimazole (tapazole®) in doses of 20 to 40 mg. daily. Both propylthiouracil and methimazole were found to be effective antithyroid agents, with a low incidence of side-reactions. Antithyroid drugs must be administered under careful observation, since

serious blood changes (agranulocytosis and granulocytopenia) are a real danger. When these drugs are used preoperatively, dosage must be determined for each patient individually and thyroidectomy should not be done until a euthyroid state is reached and all evidences of hyperthyroidism and resulting physical depletion are overcome. If this is accomplished, a low operative mortality is possible, as shown in the author's series in which there were only five postoperative deaths (0.2%), all occurring in patients with associated cardiac disease. Of the 2,400 patients, 27 were pregnant; 21 of them had normal deliveries at term yielding 23 healthy infants. Antithyroid drugs can safely be given to pregnant patients with hyperthyroidism if myxedema is avoided preoperatively and postoperatively until the time of delivery. Postoperative tetany occurred in 70 (3%) of the first 2,300 patients, and was permanent in 42 (1.8%). In all of these patients the tetany was controlled with powdered calcium lactate alone or in combination with vitamin D. Hyperthyroidism recurred, even after radical thyroidectomy, in 33 (1.9%) of the 1,670 patients who had had periodic metabolic studies for three to eight years. These patients were treated selectively; in most patients the disease was controlled either by the daily administration of iodine or by a second surgical intervention removing the recurring thyroid remnants. Postoperative myxedema occurred in 69 (7.3%) of the first 942 patients who could be followed; it was transient in 13 (1.3%) and permanent in 49 (5.2%), while 7 could not be followed adequately. Myxedema occurred any time within five years after the thyroidectomy, and it was transient up to the third year. In most patients, however, postoperative myxedema developed within the first year and remained permanent if thyroid administration was required after the first year. Desiccated thyroid controlled all cases of postoperative myxedema; the usual daily dose was 0.1 gm. (1.5 grains) or less.

Disturbance of Normal Bacterial Ecology by Antibiotics.—According to Smith, the complex balance that exists among micro-organisms that constitute the normal flora of the human body may be disturbed by prolonged administration of the newer antibiotics. This may result in development of secondary vitamin deficiencies or evolution of new infectious disease syndromes. By reviewing the literature, the author found that prolonged treatment with penicillin suppresses or eliminates gram-positive bacteria and stimulates directly or indirectly multiplication of gram-negative bacilli. Prolonged therapy with relatively large doses of streptomycin may suppress the gram-negative bacilli and stimulate the growth of gram-positive cocci. This effect is not so constant as the reversed one induced by penicillin therapy. The prolonged administration of both penicillin and streptomycin simultaneously, or of aureomycin, chloramphenicol, or oxytetracycline ("terramycin") may suppress both gram-positive cocci and gram-negative bacilli to such a degree that the fungi of the normal flora multiply and produce disease in the mouth, vagina, bronchi, lungs, and intestinal tract. The case of a 16-year-old girl with chronic bronchiectasis is reported in detail to illustrate the influence of alternate and simultaneous administration of penicillin and streptomycin on the organisms found in the sputum of this patient. Prolonged treatment with aureomycin was followed by the development of a severe secondary pulmonary moniliasis and a vitamin deficiency of the B complex type characteristic of pellagra in a 60-year-old woman, whose case is likewise reported in detail. The newer broad spectrum antibiotics should not be administered for more than one week at a time unless the agent causing the infection has been identified and the indications for prolonged treatment are obvious. A complete vitamin supplement, with special emphasis on the B complex group, should be given to all patients receiving prolonged treatment with the newer antibiotics. In addition antibiotics should not be used in mild and ill-defined infections because a drug sensitivity may develop that will prevent the subsequent use of the antibiotic in a major illness. The dangers of inducing sensitivity seem to be greatest when the antibiotic is applied locally.

Arizona Medicine, Phoenix

10:1-44 (Jan.) 1953

Cancer Detection: Realistic Appraisal of Its Value. I. Macdonald.—p. 1.
Superior Vena Cava Obstruction in Primary Cancer of the Lung. B. M. Lipschultz.—p. 10.
Surgical Pathology in Everyday Medical Practice. O. A. Brines.—p. 13.
Radioactive Iodine in Diseases of Thyroid Gland. E. W. Czerny and H. D. Cogswell.—p. 16.

Blood, New York

8:1-100 (Jan.) 1953

Function of Eosinophile Leukocyte. J. Vaughn.—p. 1.
*Mechanism of Quinidine Purpura. R. K. Larson.—p. 16.
Studies on Platelets: IX. Observations on Properties and Mechanism of Action of Potent Platelet Agglutinin Detected in Serum of Patient with Idiopathic Thrombocytopenic Purpura (With a Note on Pathogenesis of the Disease). M. Stefanini, W. Dameshek, J. B. Chatterjea and others.—p. 26.
*Demonstration of "L.E." Phenomenon in Patients with Penicillin Hypersensitivity. J. R. Walsh and H. J. Zimmerman.—p. 65.
Experimental Production of Splenomegaly, Anemia and Leukopenia in Albino Rats. J. G. Palmer, E. J. Eichwald, G. E. Cartwright and M. M. Wintrobe.—p. 72.
Treatment of Pernicious Anemia with Massive Parenteral Doses of Vitamin B_{12}. E. H. Reisner Jr. and L. Weiner.—p. 81.

Mechanism of Quinidine Purpura.—Thrombocytopenic purpura occurred in a 61-year-old woman who had been treated for paroxysmal tachycardia with quinidine sulfate in doses of 0.2 gm. four times a day for 26 days. The platelet count was 8,000 per cubic millimeter. To establish hypersensitivity to quinidine as the cause, 0.2 gm. of this drug was given to the patient orally on a fasting stomach. The number of circulating platelets rapidly decreased. This fall was too rapid to be accounted for by inhibition of the bone marrow megakaryocytes alone. Inhibition of clot retraction could be produced in vitro by the addition of minute quantities of quinidine to the patient's blood. This was assumed to demonstrate a specific peripheral action of quinidine on this patient's platelets. No inhibition of clot retraction could be produced by the addition of quinine (an optical isomer of quinidine) to the blood of this patient in vitro. This was further evidence of the pronounced specificity of the reaction. Complete inhibition of clot retraction could be produced in the blood of a normal person by the addition of serum from the patient together with quinidine. No inhibition occurred if one or the other was added alone. This was assumed to demonstrate that quinidine did not affect the platelets directly but did so through combined action with some other element in platelet-free serum. It was felt that this was strong support for an antigen-antibody type of reaction. No significant fall in platelet concentration by the addition of quinidine in vitro could be demonstrated. This was interpreted as evidence against complete lysis of the platelets as the method of destruction. The fact that the platelet count was decreased in vivo but not in vitro suggested that the platelets were injured in such a manner as to effect their rate of removal by the reticuloendothelial system and their ability to produce clot retraction. On the second day after discontinuation of quinidine therapy, the platelet count in the patient was 74,000 per cubic millimeter and by the seventh day it was 164,000 per cubic millimeter. The clinical improvement of the patient was as rapid as the rise in platelets. A platelet count done two months after discharge was 250,000 per cubic millimeter, and the patient had had no recurrence of purpura.

The L. E. Phenomenon in Penicillin Hypersensitivity.—Three of six patients with clinical evidence of untoward reactions to penicillin had a generalized, febrile illness that simulated serum sickness with severe skin lesions. Minimal urticarial lesions involving small areas of the body were the only evidence of hypersensitivity to penicillin in the remaining three patients. The three patients whose reactions to penicillin were severe were found to have the L. E. factor in the plasma and L. E. cells in the bone marrow. The other three patients failed to show the L. E. phenomenon. Since the group studied was small, no conclusions regarding the incidence of the L. E. phenomenon in untoward reactions to penicillin can be drawn. The findings are discussed in the light of the possibility that the L. E. phenomenon may be related to hypersensitivity reactions as well as to systemic lupus erythematosus.

Bulletin of Menninger Clinic, Topeka

17:1-40 (Jan.) 1953

Borderline States. R. P. Knight.—p. 1.
Chronic Cyclic Schizo-Affective Psychosis. R. A. Solow.—p. 13.
*How Common is Schizophrenia? E. A. Gaw, S. Reichard and C. Tillman. —p. 20.
Understanding and Use of the Self in Counseling. D. Johnson.—p. 29.

How Common Is Schizophrenia?—Realizing that obsessions and phobias could occur in incipient schizophrenia as well as in true neuroses, Gaw and associates began to look for slight evidences of loosening or splitting of the associations, autism, and flattening or pathological intensification of affect. They found that by combining thorough examinations, comprehensive case histories and a battery of psychological tests, the incidence of diagnoses of schizoid and schizophrenic conditions greatly increased among outpatients in their psychiatric clinic. From a perusal of Bleuler's work it became clear that, although orthodox psychiatry has taken over the word schizophrenia, it has continued to define it in terms of Kraepelin's dementia praecox, ignoring Bleuler's intention to enlarge the scope of the disease to include nonpsychotic and nondeteriorating cases. Inasmuch as Bleuler believed that such conditions as schizoid personality and preschizophrenia are really milder degrees of the same disease entity, Gaw and associates decided to substitute the designations "minimal schizophrenia" for schizoid personality, and "moderate schizophrenia" for preschizophrenia and ambulatory schizophrenia, reserving the term "severe schizophrenia" for the full-blown psychotic manifestations of the disease. After presenting examples of the types of symptoms that induced them to diagnose schizophrenia in nonpsychotic patients, the authors feel that since they have long treated nonpsychotic schizophrenics (under other diagnostic labels) with fair success, calling them schizophrenics should not create greater pessimism about their prognosis. It simply means that they now recognize in advance the nature of the disease and the dangers and difficulties inherent in the treatment of these cases. This also means that a trial analysis is no longer necessary for the purpose of determining whether the patient is schizophrenic or in danger of a psychotic break, since this can be determined beforehand by anamnesis and through psychological testing. Psychoanalytic or depth-therapy is not indicated in schizophrenics because they tend, in any case, to be inwardly oriented, and it only encourages introspection. The therapy should be "reality oriented."

California Medicine, San Francisco

77:361-432 (Dec.) 1952

Changing Concepts in Medical Treatment. C. L. Brown.—p. 361.
Evaluation of Exposure Treatment of Burns. W. S. Kiskadden and S. R. Dietrich.—p. 365.
Newer Hematinics, Their Use and Abuse. W. F. Luttgens.—p. 369.
Causalgia—Pathogenesis and Treatment. V. H. Kuenkel.—p. 374.
Postural Vertigo and Positional Nystagmus. R. Fletcher.—p. 377.
Scintigrams of Thyroid Gland: Diagnosis of Morphologic Abnormalities with I^{131}. F. K. Bauer, W. E. Goodwin, T. F. Barrett and others. —p. 380.
*Acute and Chronic Barbiturate Intoxication: Recent Advances in Therapeutic Management. E. A. Hargrove, A. E. Bennett and F. R. Ford. —p. 383.
Cortisone and Corticotropin in Allergic Disease. A. Rowe Jr. and A. H. Rowe.—p. 387.
Primary Neoplasms of Adrenal Gland: Diagnosis and Surgical Management. H. A. Davis, I. A. Fields and A. Gerber.—p. 391.
Gastroduodenostomy After Gastric Resection. R. L. Zieber and J. M. Kenney.—p. 395.
Urethral Stenosis in Young Girls: Cause of Recurrent Infection of Urinary Tract. J. W. Schulte and G. F. Williams.—p. 397.
New Vistas in Psychosomatic Medicine. A. Coodley.—p. 401.

Management of Barbiturate Intoxication.—The symptoms of severe acute barbiturate poisoning are stupor or coma, slow and shallow respiration, weak and thready pulse, dilation of pupils, flaccidity of limbs, and absence of tendon reflexes. Babinski's sign may be present, and convulsions may occur. The authors discuss the disorders that have to be considered in the differential diagnosis of acute barbiturate intoxication or addiction. An accurate history and a thorough examination, which will reveal increased nonprotein nitrogen in the blood and a characteristic fast pattern in an electroencephalogram, will help to clarify the diagnosis. In the treatment of barbiturate intoxication picrotoxin has been considered the drug of choice, but it may cause convulsions that lead to death. In 1950 Jones and co-workers recommended the use of pentylenetetrazole (metrazol®) for barbiturate poisoning, and the authors of this report have likewise found it superior to picrotoxin when administered as recommended by Jones: intravenous administration of 5 cc. of pentylenetetrazole, followed in 15 minutes, unless reflexes return, by 10 cc., and thereafter by 20 cc. every 30 minutes until the reflexes return. Small doses can then be given intramuscularly until the patient is conscious. Since the maximum effect is obtained almost immediately, there is less danger of overdosage and convulsions than is the case with picrotoxin. Robie found that nonconvulsive electrostimulation was helpful in treating patients who had taken an overdose of barbiturates. He applies an electrostimulator and maintains the current at 2 to 3 ma. until the patient begins to awaken. Antibiotics and intratracheal intubation are useful adjuncts in counteracting hypostatic and aspiration pneumonia. Carefully controlled withdrawal and psychiatric rehabilitation are necessary in the treatment of barbiturate addiction, but as patients are usually uncooperative the prognosis is poor. The addition of emetics to barbiturates might prevent overdosage and is being considered as a possible preventive measure of barbiturate intoxication and addiction.

Cancer Research, Chicago

12:847-940 (Dec.) 1952

Some Investigations on Cell Behavior Under Various Conditions: Review. H. Lettré.—p. 847.
Induction of Accessory Limbs and Sarcoma in Newt (Triturus viridescens) with Carcinogenic Substances. C. Breedis.—p. 861.
Distribution of Administered Radioactive Rubidium (Rb^{86}) in Normal and Neoplastic Tissues of Mice and Humans. A. Zipser and A. S. Freedberg.—p. 867.
Effects of Combinations of Antileukemic Agents on Acute Lymphocytic Leukemia of Mice. L. W. Law.—p. 871.
Nicotinamide Content of Some Normal and Malignant Tissues: Apparent Absence of Niacin in Epidermis. C. Carruthers and V. Suntzeff. —p. 879.
Inactivation in Vitro of Transplantable Myeloid and Lymphoid Mouse Leukemic Cells by Antibodies Produced in Foreign Host Species. A. A. Werder, A. Kirschbaum, E. C. MacDowell and J. T. Syverton.—p. 886.
Nerve Sheath Tumors in Isolated Goldfish Population. H. G. Schlumberger.—p. 890.
Neoplastic Diseases in Infants and Children. E. A. Lawrence and E. J. Donlan.—p. 900.
Influence of Dietary Casein Level on Tumor Induction with 2-Acetylaminofluorene. R. W. Engel and D. H. Copeland.—p. 905.
Heterotransplantation of Human Cancer. I. Irradiated Rats. S. C. Sommers, R. N. Chute and S. Warren.—p. 909.
Id.: II. Hamster Cheek Pouch. R. N. Chute, S. C. Sommers and S. Warren.—p. 912.
Id.: III. Chorioallantoic Membranes of Embryonated Eggs. S. C. Sommers, B. A. Sullivan and S. Warren.—p. 915.

Diseases of Chest, Chicago

23:1-120 (Jan.) 1953

*Isoniazid and Its Isopropyl Derivative in Therapy of Tuberculosis in Humans: Comparative Therapeutic and Toxicologic Properties. E. H. Robitzek, I. J. Selikoff, E. Mamlok and A. Tendlau.—p. 1.
Clinical Experiences with Isonicotinic Acid Hydrazide in Tuberculosis. E. Witkind and I. Willner.—p. 16.
Effects of Isonicotinic Acid Hydrazide in Mentally Ill Patients. A. E. Krieser, A. G. Sanderson, M. Vik and J. A. Myers.—p. 28.
Double Aortic Arch Associated with Coarctation of Aorta: Surgically Treated Patient. T. J. Dry, O. T. Clagett, R. F. Saxon Jr. and others. —p. 36.
Use of 2-Ethylhexanol in Acute Pulmonary Edema. N. E. Reich, B. A. Rosenberg and M. Metz.—p. 43.
Duration of Carcinoma of Lung. L. G. Rigler, B. J. O'Loughlin and R. C. Tucker.—p. 50.
Special Complex of Pulmonary Tuberculosis in Right Upper Lobe with Involvement of Interlobar Pleura. L. Dunner.—p. 72.
Sidero-Silico Tuberculosis in Foundry Employee. L. E. Hamlin.—p. 81.
Failure of P- (Di-N-Propylsulfamyl)-Benzoic Acid ("Benemid") to Influence P-Aminosalicylic Acid Blood Levels. C. Riley, R. A. Clowater and S. J. Shane.—p. 90.
Tribione (Amithiozone) in Pulmonary Tuberculosis. H. O. Puelma, M. Z. Granello and R. O. Cruz.—p. 94.
*Selection of Patients with Cardio-Pulmonary Diseases for Air Travel. B. Gordon.—p. 98.

Isoniazid in Treatment of Tuberculosis.—Of 175 patients with caseous pneumonic tuberculosis with cavities and sputum positive for tubercle bacilli, 101 were given iproniazid (marsilid®), in standard doses of 4 mg. per kilogram of body weight, 65

were given isoniazid (rimifon®) in doses of 4 mg. and 8 mg. per kilogram of body weight, and 9 were given combined streptomycin and iproniazid or isoniazid therapy for from two to seven months. Comparison of results obtained in these patients showed that, dose for dose, the systemic effects of tuberculosis are more promptly and more completely controlled by iproniazid than by isoniazid. Roentgen ray changes and bacteriologic examination of sputum showed approximately equal benefit. Drug toxicity was observed more frequently and more intensely with iproniazid than with isoniazid. Satisfactory results were obtained with each drug in 58 patients with various forms of extrapulmonary tuberculosis such as tuberculous laryngitis, otitis, glossitis, adenitis, and enteritis. The combination of streptomycin with either isoniazid or iproniazid appeared to be superior to either drug alone on the basis of a short term study in nine cases. Clinical resistance to hydrazide therapy was not impressive. The first 17 patients under treatment for from 42 to 277 days, with an average of 112 days, continued to show in vitro sensitivity with one exception. Optimum dosage and dosage regimen for isoniazid has not been determined but is believed to be in excess of 8 mg. per kilogram of body weight in divided doses.

Cardiopulmonary Diseases and Air Travel.—Of 28 patients with cardiopulmonary disease who had been surveyed to determine the incidence of untoward effects of air travel on their condition, 25 arrived safely and comfortably at their destination. Three patients, one with spontaneous pneumothorax, one with emphysema associated with failure of the right side of the heart, and one with emphysema who had pronounced distention of the stomach with vomiting and dehydration, left the airplane because of sickness. All were treated by local physicians, and travel was resumed by land. It is significant to point out that the patient with pneumothorax traveled unexpectedly part distance in a nonpressurized airplane. The transportation by air of patients with cardiopulmonary disease is satisfactory and usually agreeable, providing the distance is sufficient to justify the long trip to and from airports. In any event, traveling should be in pressurized cabins only, since the lower barometric pressure of the ordinary types may cause symptoms of oxygen deficiency. The contraindications to air travel are cystic disease of the lung, recurrent spontaneous pneumothorax, high pressure artificial pneumothorax, acute upper respiratory tract infections with exacerbations of chronic lung disease, manifest coronary insufficiency, failure of the right side of the heart, and recent hemoptysis.

Gastroenterology, Baltimore

22:519-668 (Dec.) 1952

Pancreas: Contributions of Clinical Interest in 1951. R. Elman and L. Hollender.—p. 519.
Experiences with Use of Corticotropin in Regional Enteritis. W. G. Sauer, P. W. Brown and W. H. Dearing.—p. 550.
Potassium Balance in Ulcerative Colitis. H. M. Pollard and R. J. Bolt. —p. 564.
*Use of Cation Exchange Resin in Treatment of Ascites and Edema in Cirrhosis of Liver. B. D. Rosenak, R. H. Moser, R. D. Pickett and others.—p. 575.
*Effectiveness of Balarsen (Mercaptoarsenol), in Treatment of Amebiasis. J. S. Levy and R. W. Talley.—p. 588.
Necrotizing Typhlitis Associated with Blood Dyscrasias. J. D. MacCallum, W. M. Chardack and F. S. Schwarz.—p. 598.
Spasm of Choledochal Spincter Accompanying Sudden Stress. W. H. Bachrach, J. L. Smith and J. A. Halsted.—p. 604.
Investigation of Permeability Factor in Ascites and Edema Using Albumin Tagged with I^{131}. J. A. Schoenberger, G. Kroll, A. Sakamoto and R. M. Kark.—p. 607.
Studies in Gastric Secretion: Attempts to Produce Histamine in Vivo as Secretory Stimulant. I. H. Einsel, E. N. Nixon and J. M. Rogoff. —p. 623.
Cholangiolitic Biliary Cirrhosis with Short Fatal Course. W. E. Ricketts. —p. 628.

Use of Cation Exchange Resin in Ascites and Edema.—Sodium retention is a factor in the production of ascites in cirrhosis. The coexistence of hypoalbuminemia and a tendency to retain sodium presents a difficult problem, and so it was decided to administer a diet ample in protein and calories but restricted in sodium and to prevent the absorption of sodium from the gastrointestinal tract by the simultaneous ingestion of a sodium-removing resin. The resin used was a mixture, of which 59% was in the form of a carboxylic type cation exchanger in the hydrogen cycle, 29% was in the form of the potassium salt, and 12% was a weakly basic polyamine anion exchange resin. A portion of the resin is supplied in the potassium cycle to prevent deficiency of this ion. Prompt disappearance of ascites occurred in 17 of the 24 patients treated, and improvement occurred in 4 additional patients. Hypopotassemia and acidosis were the most important complications, but it was never necessary to stop treatment because of acidosis. The addition of potassium to the resin has reduced the danger of hypopotassemia considerably, but it is still possible that hypopotassemia may develop. It should be confirmed by an electrocardiogram. The administration of potassium by mouth or by infusion combats the deficiency. In rare instances hyponatremia may develop as a result of strict limitation of salt in the diet and ingestion of the sodium-removing resin. This condition must also be suspected from symptoms. It is rapidly responsive to administration of sodium chloride. Complications are most likely to occur if the patient is not ingesting the prescribed diet. Patients should not take the resin if they are unable to take their full diet. The laboratory tests required for the control of resin therapy include determination of plasma carbon dioxide and chlorides, electrocardiograms, and, in special instances, determination of plasma potassium and sodium levels. The employment of these controls and cooperation of the patient make the use of sodium-removing resin a valuable adjunct in selected cases.

Mercaptoarsenol in Treatment of Amebiasis.—Since none of the drugs in common use for amebiasis have proved completely satisfactory, Levy and Talley used a new arsenical mercaptoarsenol ("balarsen"), which was developed for the treatment of yaws. It is a cyclic arsenical compound (N-2-acetylamino-4 methylol-cyclo-ethylene dimercapto arsinephenol) prepared from the interaction of 3-acetylamino-4-hydroxy phenylarsenoxide and mercaptopropanol. Animal studies demonstrated a low toxicity for mice, rats, and guinea pigs. Patients with either the cysts or the trophozoites of Endamoeba histolytica in the stool were given mercaptoarsenol in doses of 10 to 20 mg. per kilogram of body weight to a maximum of 1 gm. daily, for five successive days. When possible, the patients were hospitalized. Daily stool examinations were made during treatment and for four to seven days following the last dose. Those not hospitalized were examined a day or two after the five day course of treatment had been completed. Sigmoidoscopic examinations were made at completion of treatment and on follow-up visits. Patients were requested to return at monthly intervals. Cysts alone were found in 10 of the 25 patients with amebiasis, cysts and trophozoites in 13, and trophozoites alone in 2. Seven patients had been treated previously for amebiasis. Mercaptoarsenol was effective in 23 of 25 cases with one five-day course of therapy. A second course of treatment (one of 5 days and one of 10 days) was effective in the two cases in which stools were still positive after the first course. Eleven of 12 patients followed for one full year had negative stools at the end of the year. These results compare favorably with those of other drugs, and mercaptoarsenol has the advantages of a short course of therapy, ease of administration, low toxicity, and inexpensiveness.

Journal Clin. Endocrin. & Metab., Springfield, Ill.

12:1513-1642 (Dec.) 1952

Urinary Estrogens (Measured Fluorometrically and Biologically) in Hyperadrenocorticism: Influence of Cortisone, Compound F, Compound B and ACTH. C. J. Migeon and L. I. Gardner.—p. 1513.
Effects of Chorionic Gonadotropin (APL) in Male "Eunuchoidism with Low Follicle-Stimulating Hormone": Aqueous Solution Versus Oil and Beeswax Suspension. F. C. Bartter, R. C. Sniffen, F. A. Simmons and others.—p. 1532.
Excretion of 17-Ketosteroids: II. Values in Several Endocrine Disturbances. S. Kenigsberg and T. H. McGavack.—p. 1551.
Graves' Disease: Hyperthyroidism or Hyperpituitarism? S. C. Werner, H. Hamilton and M. Nemmeth.—p. 1561.
Serum Protein-Bound Iodine During Ingestion of Desiccated Thyroid. T. S. Danowski, S. J. Huff, R. Tarail and others.—p. 1572.
*Chronic Thyroiditis: Clinical and Pathologic Study of 354 Patients. S. Lindsay, M. E. Dailey, J. Friedlander and others.—p. 1578.

Chronic Thyroiditis.—Chronic thyroiditis, as evidenced by lymphoid infiltration, fibrosis and epithelial alteration of the thyroid gland, is a poorly defined disorder. It was present in 195 (3%) of 6,571 thyroid glands removed at the University of

California Hospital from 1920 to 1950. The pathological diagnosis in 170 of these 195 glands was lymphadenoid goiter, also known as Hashimoto's thyroiditis or struma lymphomatosa; in 23 it was granulomatous or giant-cell thyroiditis; and in two Riedel's type of thyroiditis. Lymphadenoid goiter or Hashimoto's thyroiditis is characterized by epithelial degeneration followed by follicular regeneration and reorganization, associated with varying degrees of lymphoid infiltration and fibrosis. The pathological picture first described by Hashimoto represents only one phase or variant of the disease. This lesion may progress to extensive replacement of the thyroid gland by fibrous tissue. Granulomatous or giant-cell thyroiditis is an acute necrosis of thyroid follicular epithelium associated with acute and chronic inflammation, followed by fibrosis and follicular regeneration and reorganization. This disease has been described previously by DeQuervain and Giordanengo, Crile, and others. "Riedel" thyroiditis is characterized by pronounced fibrous invasion of the adjacent cervical tissues. In addition to the 195 thyroid glands that displayed the three types of diffuse thyroiditis, the authors also studied 159 glands in which the basic pathological patterns of lymphadenoid goiter were focal or were accompanied by hyperplasia, involutional nodules, or benign or malignant neoplasms. It was concluded that these thyroid diseases have a close relationship to thyroiditis of the "Hashimoto" type. There is a significantly greater incidence of malignant thyroid neoplasms in glands with this type of thyroiditis than in those free of the inflammatory disease. In all three types of chronic thyroiditis there may be hard, fibrous thyroid glands that adhere to adjacent structures. The type classified as "Riedel" thyroiditis is the only one characterized by invasive adherence of the gland to surrounding tissues.

Journal Nat. Cancer Inst., Washington, D. C.

13:577-772 (Dec.) 1952. **Partial Index**

Review of Cancer Control Problem. J. R. Heller.—p. 577.
Review of Some Spontaneous Tumors in Noninbred Mice. H. A. Horn and H. L. Stewart.—p. 591.
Splenomegaly with Excess Numbers of Kurloff Cells in Guinea Pigs Treated with Stilbestrol. E. M. Nadel.—p. 605.
Action of BAL on Tumor-Damaging Potency of Certain Trivalent Arsenic Compounds. L. V. Beck.—p. 619.
Some Observations on Volume of Nucleus of Spontaneous Hepatomas in Mice. T. Miyaji.—p. 627.
Histogenetic Classification of Induced Gastric Sarcoma in Mice. E. A. Saxén and H. L. Stewart.—p. 657.
Induction of Pulmonary Tumors in Guinea Pigs by Intravenous Injection of Methylcholanthrene and Dibenzanthracene. W. E. Heston and M. K. Deringer.—p. 705.
Enhancement and Inhibition of Growth of Tumor Homoiotransplants by Pretreatment of Hosts with Various Preparations of Normal and Tumor Tissue. G. D. Snell.—p. 719.
*Estrogen-Induced Tumors of Kidney: I. Incidence of Renal Tumors in Intact and Gonadectomized Male Golden Hamsters Treated with Diethylstilbestrol. H. Kirkman and R. L. Bacon.—p. 745.
Id.: II. Effect of Dose, Administration, Type of Estrogen, and Age on Induction of Renal Tumors in Intact Male Golden Hamsters. H. Kirkman and R. L. Bacon.—p. 757.

Incidence of Estrogen-Induced Tumors of Kidney.—The occurrence of renal cortical tumors in estrogen-treated golden hamsters (Cricetus auratus) has been described in earlier reports. In this paper Kirkman and Bacon are concerned with the incidence of these tumors. Intact male golden hamsters, treated continuously with diethylstilbestrol (0.6 mg. in sesame-oil solution or in saline suspension injected subcutaneously every other day, or subcutaneously implanted pellets), showed no renal tumors in less than 150 days of treatment (12 animals). Tumors did develop in one animal of 10 treated for 150 to 199 days, in six of nine animals, treated for between 200 to 249 days, and in 97 of 100 animals treated for 250 days or longer. One of the animals treated for 229 days and 44 of those treated for 250 days or longer showed metastases. Metastases did not occur outside of the abdominal cavity, although the tumor cells have been shown to be capable of metastases through the blood and lymph streams. Renal tumors developed in all of 18 castrated hamsters treated similarly with diethylstilbestrol for 248 to 415 days. Three of the 18 tumors metastasized.

Journal of Thoracic Surgery, St. Louis

24:545-650 (Dec.) 1952

*Silicotic and Tuberculosilicotic Lesions Simulating Bronchogenic Carcinoma. F. G. Kergin.—p. 545.
*Nodular Tuberculosis. D. O. Shields, J. S. Chapman Jr., J. Carswell Jr. and O. J. Wollenman.—p. 568.
Complications and Results of Treatment of Bronchopleural Fistula Following Resection for Tuberculosis. J. D. Murphy, B. B. Becker and H. V. Swindell.—p. 578.
Plastic Sponge Prosthesis Following Resection in Pulmonary Tuberculosis. J. W Gale, A. R. Curreri, W. P. Young and H. A. Dickie.—p. 587.
Circulatory Arrest. V. O. Björk.—p. 611.
*Atelectasis: Physiopathology and Treatment: Special Reference to Its Occurrence in Bulbar Poliomyelitis, and to Suggested Therapeutic Aid by Intrabronchial Administration of Trypsin. M. E. Peck and S. Levin.—p. 619.
Concurrent Lymphoma of Lung and Stomach: Follow-Up on Previously Reported Case. P. L. Shallenberger, P. Fisher, W. C. Beck and C. H. DeWan.—p. 637.

Silicotic and Tuberculosilicotic Lesions.—The appearance of unilateral massive densities in the lung of eight men between the ages of 49 and 69 with chronic pneumonitis has been reported. In each of these patients clinical and radiographic evidence strongly suggested a diagnosis of bronchiogenic carcinoma. Five of the eight patients had prolonged exposure to dust, three as foundry workers, one as a grinder, and one as a miner. One of the other three had worked underground as a miner without direct exposure, one had been a sandblaster for a year 34 years previously, and one had been a driller in a hard rock mine for two years 38 years previously. Five patients were treated by pneumonectomy and one by lobectomy. In another thoracotomy was done, and biopsies were made. The eighth patient has not been operated on. A study of the excised tissue indicated that the fundamental feature of the pathological processes in this group of patients is complete or partial bronchial obstruction by pressure of lymph nodes, which are the site of a chronic inflammatory reaction secondary to inhalation of silica-containing dust. In five patients the chronic obstructive pneumonitis was nonspecific, and in three there was an added tuberculous infection. It is suggested that this condition be called "chronic silicotic lymphadenitis with obstructive pneumonitis (nontuberculous or tuberculous)." The patients are all alive; the six patients treated by excision have been relieved of their complaints.

Nodular Tuberculosis.—Of 140 patients with nodular tuberculosis studied by the authors, 49 had residual nodules left from clearing tuberculous pneumonia, 31 had nodules of undetermined origin, 10 had nodules developing from inspissated cavities, 4 had true tuberculomas, and 46 had multiple nodules with fibrosis. With the exception of the small group with true tuberculomas, all the other groups were followed for an average of four years. The tuberculosis was reactivated in 35 (25%) of the 140 patients. The reactivation rate was high in the group with inspissated cavities and in that with multiple nodular disease, but was relatively low in the patients with nodules of undetermined origin of development and in those with a few residual nodules from tuberculous pneumonia. Of 18 patients who received collapse therapy, 11 were treated by a phrenic crush and 4 of these had reactivation; 7 were treated by pneumothorax and 4 of these had reactivation. Only 2 patients had reactivation of 30 who submitted to lobectomy, segmental resection, and wedge or local resection and were followed for an average of 27 months. Although it is dangerous to make generalizations concerning tuberculosis, the reported data suggest that collapse therapy does not prevent reactivation of nodular tuberculosis and that resection may be a valuable therapeutic procedure in treatment of this type of tuberculosis. The authors believe that resection of nodular tuberculosis should usually be restricted to inspissated cavities and multiple nodular tuberculosis.

Atelectasis.—According to Peck and Levin, the development of atelectasis in a lung, lobe or segment depends on the presence of some mechanical cause of obstruction, sufficient circulation to allow absorption of the air distal to the obstruction, and the absence of accessory means for air entry into the distal portions of the obstructed area. Atelectasis is normally prevented by the following physiological mechanisms: efficient

ciliary action on a normal bronchial mucous membrane, a normal exudate from the bronchial mucosa, an efficient collateral respiration, an efficient cough mechanism, and absence of infection in the tracheobronchial tree. Management of the patient with atelectasis should be directed at removal of the obstructing agent, loosening and removal of viscid bronchial secretions, establishment of an efficient collateral respiration, assistance in the securing of a good cough, and treatment of any incipient infection. "Tryptar," a proprietary preparation of purified crystalline trypsin, was used as an enzymatic agent for physiological débridement in four patients with atelectasis, two of whom had poliomyelitis. In these two bronchoscopy alone had failed to remove the obstruction. A standard dilution consisting of 250 mg. of trypsin in 5 cc. of Sorensen's phosphate buffer solution was slowly introduced through the branch oxygen inlet of the bronchoscope, which had been passed into the main stem bronchus of the dependent side after all endobronchial secretions had been aspirated from both main stem bronchi and all orifices. The trypsin was aspirated into all segmental bronchial orifices. The scope was then removed and the patient kept in the same position for an hour, after which all secretions were again aspirated with the bronchoscope. An additional measure of value was the use of an exsufflator attached to a tank-type respirator or to a pressure hood. By this means a high rate of air flow during expiration, equivalent to a moderately vigorous cough, can be obtained. It is suggested that three to five one-half hour exsufflator treatments a day for two to five days may be required to accomplish complete aeration of the lungs and disappearance of atelectasis. Large doses of penicillin were given to control infection. Detailed case reports of the two patients with poliomyelitis illustrate the successful use of trypsin in relieving chronic atelectasis due to bronchial and bronchiolar obstruction in patients with bulbar poliomyelitis. It is urged that further experience be accumulated on the effectiveness of endobronchial application of trypsin in relieving persistent atelectasis in carefully selected patients.

Maryland State Medical Journal, Baltimore

1:579-642 (Dec.) 1952

Geriatrics in General Practice. W. M. Johnson.—p. 582.
Cholecystography Using Telepaque. H. F. Zangara, C. N. Davidson and W. L. Kilby.—p. 593.

New England Journal of Medicine, Boston

247:1003-1050 (Dec. 25) 1952

Cardiac Arrest in Operating Room: Report of Five Cases Occurring in Community Hospital. P. R. Hinchey and C. J. Straehley Jr.—p. 1003.
Oral Use of Fat Emulsions in Clinical Medicine. M. Shoshkes.—p. 1010.
*Thrombectomy in Volkmann's Contracture. D. K. Crystal, E. Burgess and C. Wangeman.—p. 1015.
*Hemigastrectomy Combined with Resection of Vague Nerves. D. A. Farmer and R. H. Smithwick.—p. 1017.
New Technics and Materials in Upper-Extremity Prosthetics. A. Thorndike.—p. 1022.
Chills and Fever Due to Procaine Amide Hydrochloride Therapy. J. J. McGarry.—p. 1033.
Choleresis in Hyperacidity and Peptic Ulcer. F. W. Palfrey.—p. 1034.

Thrombectomy in Volkmann's Contracture.—A 3-year-old girl sustained a supracondylar fracture of the right humerus on May 12, 1950. The fracture was reduced one hour later. About 4 hours later the radial pulse was absent and the hand was slightly swollen and cold. The arm was removed from the splint and placed in extension, and an incision was made across the antecubital space and the lacertus fibrosus. The brachial artery was pulseless, but perivascular stripping caused the artery to dilate somewhat and even brought about a feeble pulsation in the radial and ulnar arteries. About 20 hours after injury, the hand was drawing upward in volar flexion, there were no pulses at the wrist, voluntary motion was absent, and passive extension of the hand caused severe pain. The incision was reopened, revealing the constricted brachial artery, with pulsations visible only in the proximal portion of the artery. No pulsations were palpable in the two principal branches. A thrombus was suspected at the site of greatest trauma to the artery. The artery did not bleed when first opened. Gentle compression distal to the incision caused extrusion of a clot 7 by 2 mm. Free bleeding was permitted for 2 minutes. The vessel was closed by a single everting mattress suture. Pulsation became visible in the distal brachial artery and in its branches, the radial and the ulnar arteries. The hand became pink and warmer. At the time of writing, 27 months later, the child used her hand normally; there was, however, some atrophy of the hand, which was most noticeable in the volar digital pads at the ends of the fingers, but improvement was continuing. This case provides a challenge to reexamine current surgical thought concerning Volkmann's contracture, and to recall that Volkmann in his original discussion referred to it as an "ischemic" contracture. Experience in World War II tends to reemphasize the importance of arterial obstruction as opposed to venous thrombosis. A direct attack on the artery is advisable in the relief of acute devastating vascular constriction.

Hemigastrectomy Combined with Resection of Vagus Nerves.—In recent years Farmer and Smithwick have combined hemigastrectomy with resection of the vagus nerves in 40 patients with duodenal ulcer. Detailed studies of the acidity of the gastric contents were carried out before and at intervals after operation. The findings are compared with those obtained after subtotal gastrectomy alone and combined with vagotomy, vagotomy combined with resection of the distal third of the stomach, and vagotomy combined with posterior gastroenterostomy, and also with the results in 17 patients with gastrojejunal ulceration after various operations. Achlorhydria under fasting conditions and on stimulation by beef broth and insulin occurred more frequently after hemigastrectomy combined with resection of the vagus nerves than after any other procedure employed. Achlorhydria should theoretically occur at least as frequently after subtotal gastrectomy combined with vagotomy as after hemigastrectomy combined with vagotomy. That this was not so in the series studied is explained by the fact that two of eight patients with subtotal gastrectomy had incomplete nerve sections, whereas only 3 of 40 patients who had hemigastrectomy proved to have incomplete nerve sections. These results suggest that hemigastrectomy combined with vagotomy will afford the patient with duodenal ulcer greater protection against recurrent ulceration than vagotomy combined with gastroenterostomy, than removal of less than half the stomach, or than subtotal gastrectomy alone. Hemigastrectomy combined with vagotomy has been followed by a lower incidence of unpleasant postoperative side-effects than subtotal gastrectomy alone or combined with resection of the vagus nerves. When evaluated on the basis of both the physiological effects and the clinical results, hemigastrectomy combined with vagotomy has so far given the best results.

New Orleans Medical and Surgical Journal

104:735-790 (Dec.) 1952

Obstruction of the Colon. G. V. Brindley.—p. 735.
Incidence and Types of Salmonella Infections in Louisiana. G. H. Hauser and L. Godelfer.—p. 744.
Management of Acute Ankle Fractures. M. M. Bannerman and T. Campanella.—p. 748.
Radiation Therapy in Carcinoma of the Cervix. D. S. Carnahan Jr.—p. 750.
*Effect of Hyaluronidase on Protective Urinary Colloids and Its Significance in Treatment of Renal Lithiasis. A. J. Butt, J. Seifter and E. A. Hauser.—p. 754.
Value of Bronchography. E. H. Little.—p. 758.
Role of Private Physician in Tuberculosis Control. C. C. Aven.—p. 763.
Field of General Practice. P. Williamson.—p. 764.
Criminal Abortion. V. A. Culotta.—p. 766.
Postpartum Eclampsia. H. J. Tatum.—p. 769.

Hyaluronidase in Treatment of Renal Lithiasis.—In patients receiving hyaluronidase to facilitate hypodermoclysis, it was observed that cloudy urines were clarified. Seifter suggested that hyaluronidase acted by the release of hyaluronic acid at the site of injection with subsequent excretion in the urine. This hypothesis has been confirmed by Hauser's studies, including ultramicroscopic observations that (1) potassium hyaluronate added to voided urine acts as a powerful dispersing or peptizing agent and (2) the subcutaneous injection of hyaluronidase mixed with isotonic sodium chloride solution results

in release of a protective colloid into the urine that inhibits formation of new crystalline material and disperses crystalline matter already present. Hyaluronidase therapy has been used in 24 patients with rapidly recurring renal calculi. No treatment had been effective before hyaluronidase was used. Dosages used were 150 to 600 turbidity reducing units, repeated on the average of 24 to 72 hours. In 19 patients, no new stone formation or increase in size of existing stones occurred during a period of 11 to 21 months, as demonstrated by x-rays taken at 30 to 60 day intervals. In 4 of the 24 patients there was evidence of reduction in size and density of the stones. In one case there was complete disappearance of multiple, bilateral small calyceal stones. Generally, the smaller the stone initially the more effective hyaluronidase therapy is in preventing its growth. In an addendum the authors say that, since presentation of this paper, they have found that larger doses of hyaluronidase, 300, 600, 900 turbidity reducing units daily, are more effective than previously prescribed dosages.

North Carolina Medical Journal, Winston-Salem

13:645-700 (Dec.) 1952

Growth of School Children as an Index of Undernutrition in the Community. A. H. Bryan.—p. 645.
Necrotizing Glomerulonephritis in Polyarteritis Nodosa: Report of Case. T. N. Lide and J. C. Wiggins Jr.—p. 651.
Case Illustrating Morphologic Difficulties Encountered in Nephrotic Syndrome. R. W. Prichard.—p. 657.
Primary Hyperparathyroidism Masked as Primary Renal Disease with Hypertension. G. J. Race.—p. 659.
Toxic Lesions Associated with Para-Aminobenzoic Acid. B. F. Fetter.—p. 663.
Electrocardiography in General Practice. D. N. Stewart.—p. 666.
Recurrent Pneumothorax Associated with Hereditary Deforming Chondrodysplasia: Report of Case Apparently Due to Puncture of Lung by Exostosis of Rib. R. C. Pollitzer, G. T. Harrell and R. W. Postlethwait.—p. 668.
Severe Choreic States in Adults as Manifestations of Depressive Reactions. W. E. Wilkinson and L. B. Hohman.—p. 674.
Aplastic Anemia with Questionable Relation to Chloromycetin Therapy: Report of Two Cases. J. L. Cochran Jr.—p. 676.

Ohio State Medical Journal, Columbus

49:1-92 (Jan.) 1953

Quinidine in Treatment of Chronic Auricular Fibrillation. G. S. Belaval and H. J. Barker.—p. 25.
Management of Herniated Intervertebral Lumbar Disc. W. M. Hegarty and C. W. Elkins.—p. 33.
Epipharyngeal Crypts. W. J. Loeb.—p. 38.
Lymphogranuloma Venereum Rectal Stricture Cured with Aureomycin. L. O. Baumgardner.—p. 41.

Postgraduate Medicine, Minneapolis

13:1-88 (Jan.) 1953

Prevention of Blindness Due to Glaucoma. R. E. Prindle.—p. 2.
Method of Diagnosis in Renal Tumors. W. M. Baurys.—p. 9.
The Acute Abdomen: Age and Frequency of Incidence as Aids in Establishing Diagnosis. D. M. Clough.—p. 19.
Eczematous Dermatitis of Hands Due to Food Allergy: Practical Outpatient Approach. J. M. Flood.—p. 26.
The Irritable Bowel Syndrome. P. L. Shallenberger and P. B. Kerr.—p. 32.
Fractures Involving Distal Epiphysial Cartilage of Radius. W. E. Dotter.—p. 39.
Volvulus of Midgut in Adult Due to Nonrotation of Intestine. J. S. Niles—p. 45.
Neurosurgical Disorders Occurring in Infants and Children. A. B. King—p. 57.
Parenteral Fluid Therapy in Pediatric Patients. W. A. Fisher and D. S. Motsay.—p. 70.

Public Health Reports, Washington, D. C.

67:1161-1264 (Dec.) 1952. Partial Index

Obstacles to Eradicating Congenital Syphilis. J. J. Wright, C. G. Sheps, E. E. Taylor and A. J. Gifford.—p. 1179.
Influenza Study Program in United States. D. J. Davis.—p. 1185.
Establishing Housing Standards for the Aged. J. Masur.—p. 1192.
*Radioactive Waste Disposal. C. C. Powell and H. L. Andrews.—p. 1214.
New York State Cancer Control Program. V. H. Handy and P. R. Gerhardt.—p. 1225.

Radioactive Waste Disposal.—With increased use of reactor-produced isotopes, many organizations must dispose of radioactive waste materials. Many of the materials are either too active to put into municipal sewer lines or are in forms not suitable for liquid disposal. Land burial is generally undesirable. Extreme care must be taken to avoid seepage and contamination of surface or ground water. The National Institutes of Health decided on burial at sea as the most satisfactory method of ultimate disposal for all radioactive wastes that cannot safely be admitted to the municipal sewage system. Two types of containers, steel drums and garbage cans, were judged unsuitable for radioactive waste disposal at sea because they roll if placed on their sides, are inconvenient to handle, and will disintegrate rapidly in sea water. Standard, commercially available, concrete burial vaults were found to be satisfactory basic containers. Child-size vaults, 19¾ by 18¾ by 44 in. (outside dimensions), hold about 5.3 cubic feet of material. As waste products are brought in from the various laboratories, monitors pack them in the vault as compactly as possible. Dilute solutions may be concentrated by chemical reactions, evaporation, or ion exchange columns before disposal. Contaminated pieces of furniture, such as hoods, are taken apart for more compact stowage. Relatively active materials are placed near the center of the vault to reduce the radiation level at the outside by both distance and shielding. When a load of from 10 to 20 tons has accumulated, the vaults are trucked to Coast Guard moorings. The vaults are loaded from the pier to the deck of a Coast Guard cutter, using the ship's cargo winch for hoisting. The load is put overside in not less than 1,000 fathoms of water, from 75 to 100 miles off shore. Since the seal between the cement cap and the body of the vault is probably not watertight, there will undoubtedly be a slow diffusion of material through this joint. Contamination by diffusion should be very small, and dilution by surrounding sea water very great.

Surgery, Gynecology and Obstetrics, Chicago

96:1-104 (Jan.) 1953

Method for Surgical Closure of Interauricular Septal Defects. R. E. Gross, E. Watkins Jr., A. A. Pomeranz and E. I. Goldsmith.—p. 1.
Retrograde Intramural Spread of Carcinoma of Rectum and Rectosigmoid: Microscopic Study. E. A. Quer, D. C. Dahlin and C. W. Mayo.—p. 24.
*Results in Treatment of Carcinoma of Colon and Rectum: Analysis of 2,341 Cases Over a 35 Year Period with 5 Year Survival Results in 1,667 Patients. R. S. Grinnell.—p. 31.
Brachial and Antebrachial Arterial Patterns: Study of 750 Extremities. L. J. McCormack, E. W. Cauldwell and B. J. Anson.—p. 43.
Use of Tracheotomy in Treatment of Crushing Injuries of the Chest. B. N Carter and J. Giuseffi.—p. 55.
Effect of Cortisone on Prevention of Peritoneal Adhesions. C. A. Hubay, E. C. Weckesser and W. D. Holden.—p. 65.
*Preinvasive Carcinoma of Cervix During Pregnancy. R. R. Greene, B. M. Peckham, J. T. Chung and others.—p. 71.
Abdominal Aortic Aneurysm: Report of Case Treated with Reactive Cellophane. W. R. Wilkinson.—p. 82.
Use of Maximal Size Vena Cava Autografts to Bridge Experimental Aortic Defects in Dogs: I. Studies of Collateral Circulations and Venous Pressure Following Resection of Long Segments of Inferior Vena Cava. R. A. Nabatoff, A. S. W. Touroff, M. Gross and S. Brahms.—p. 87.
Experimental Study on Reduction of Ureteral Reflux. I. T. Rieger and J. Harris.—p. 93.
Ankle Mortise Injuries. V. Mayer and S. Pohlidal.—p. 99.
Congenital Anomalies of First Branchial Cleft. R. M. Rankow and J. M. Hanford.—p. 102.
Management of Thromboembolic Disease in Surgical Patients. A. W. Allen.—p. 107.
Cytologic Studies in Malignant Lesions of the Vagina: I. Primary Squamous Cell Carcinoma. W. K. Cuyler, L. A. Kaufmann, L. Palumbo and B. Carter.—p. 115.

Results in Treatment of Carcinoma of Colon and Rectum.—Grinnell reviews the results of treatment of 890 patients with carcinoma of the colon and 777 patients with carcinoma of the rectum hospitalized between 1916 to 1945, inclusive. The resectability rate for colon tumors rose from 50% for the 1916 to 1920 period to 92.1% for the 1945 to 1950 period, and the operative mortality fell from 31.3 to 5.3% for these same periods. For rectal tumors the resectability rate rose from 65.7% to 83.3% and the operative mortality fell from 40.9 to 6.7%. The absolute five year survival rate for patients with carcinoma of the colon was 27.4%; for patients with carcinoma of the rectum it was 25.6%. The five year survivals following curative colon resection were very similar for the right and left colon. The poorest results were obtained in tumors of the hepatic flexure because of early spread to the liver and duodenal area.

The resectability rate of these tumors was also much lower than for other segments of the colon. The five year survival rate for patients who were treated by curative colon resection from 1936 to 1945 and survived operation was 67.9% for those without node metastasis and 36.7% for those with node metastasis. The rate for patients treated by curative abdominoperineal and perineal proctectomy was 67.4% for those without metastasis and 34.6% for those with metastasis. The five year survival rate for 53 patients with carcinoma of the rectum treated by colostomy and perineal proctectomy from 1916 to 1945 was 32.1%. The rate was approximately 13% lower than that following abdominoperineal resection over a similar period. Although the absolute five year survival rate of patients with large bowel cancers has risen in the past 30 years, chiefly because of the rise in resectability and the fall in operative mortality, there is little evidence of any recent improvement in the surgical attack on the cancer itself. The drop in the survival rate in the last five year period may be caused in part by attempts at curative resections on advanced tumors that were really not curable by surgery. The authors feel, however, that they should not be deterred from continuing to do radical resections on tumors the curability of which is undetermined.

Preinvasive Carcinoma of Cervix During Pregnancy.—Some observers reported that lesions diagnosed as preinvasive carcinoma of the cervix during pregnancy disappeared spontaneously at the termination of pregnancy, the inference being that these were "pregnancy changes" and not true preinvasive carcinoma. Greene and his associates, however, do not believe that pregnancy causes specific changes in the cervical epithelia. They grant that metaplasia and hyperplasia of glandular elements is commoner and more prominent during pregnancy than in the nonpregnant state; and that the surface stratified squamous epithelium of the cervix grows rapidly during pregnancy and that a mild increase in the thickness of the basal cell layer with normal nuclei is occasionally seen. They believe that when the criteria are present for the diagnosis of preinvasive carcinoma, this diagnosis should be made whether the patient is pregnant or not. They feel that this controversy on preinvasive carcinoma in pregnant patients can only be settled by deliberately following patients with such lesions and determining whether these lesions disappear with the termination of pregnancy. They diagnosed preinvasive carcinoma of the cervix from biopsies of 14 pregnant patients. These patients were followed through pregnancy and the puerperium. The lesion persisted after the termination of pregnancy in 12 of the 14 patients and was found in biopsies and/or operative specimens. Thus, with two exceptions, these lesions whether they were true carcinoma or not, were not "pregnancy changes" and did not disappear but persisted after termination of the pregnancy. In 2 of the 14 instances the authors were unable to find any abnormality post partum, and they feel that it is possible that the lesion was not a true preinvasive carcinoma and that it was a reversible change. Four quadrant biopsies were done twice post partum on each of these patients, and they are to be followed further. In one of these two patients the smear was positive at the time of the first postpartum biopsy (17 weeks) but negative at 31 weeks.

Texas State Journal of Medicine, Fort Worth

48:791-844 (Dec.) 1952

Urinary Obstructions in Children. G. F. Begley.—p. 795.
Use of Gastric Distention as Aid to Pediatric Urography. D. H. Allen.—p. 802.
Epidemic of Acute Nephritis in South Texas. E. E. Miller.—p. 805.
Swellings of Scrotum and its Contents: Differential Diagnosis and Management. H. M. Spence and A. Shannon.—p. 808.
Pulmonary Histoplasmosis. D. Jackson.—p. 812.
Physiologic Basis and Clinical Application of Some Tests of Liver Function. E. R. Hayes.—p. 816.
*Bagasse Disease of the Lungs: Brief Review of Literature and Report of Two Cases. S. McDaniel and J. G. Hull.—p. 820.
Massive Rupture of the Liver. T. H. Thomason.—p. 824.
Double Contrast Manifestations of Nonpolypoid Colon Diseases. C. A. Stevenson and M. Wilson.—p. 826.

Bagasse Disease.—Two cases of bagasse disease are described. The first, a man, aged 48, began working as an occasional grinder of sugar cane bagasse in August, 1949, and became a full-time worker in January, 1951. One month later fatigue, cough, dyspnea, and generalized weakness became prominent. A respiratory wheeze with paroxysmal cough productive of mucopurulent sputum was apparent in March. In May a low-grade fever with night chills and weight loss of 20 lb. (9 kg.) over a five week period forced him to discontinue his work. Examination revealed diffuse, coarse rales throughout both lung fields. A pleuritic pain was present over the right side of the chest posteriorly. A chest roentgenogram indicated diffuse infiltration throughout both lung fields. Several months later there was striking improvement with no discernible abnormality except for increased density of the markings at the right apex. The second patient was a 27-year-old man, who, after eight months of intermittent work, involving chopping bagasse bales and feeding the grinding machines, observed progressive dyspnea, pain in the anterior part of the chest, a morning cough, whitish sputum, fever, and weight loss of 15 lb. (6.8 kg.). Some months after he ceased working with bagasse, his condition improved. Bagasse disease is a grave industrial hazard, 4 persons having died of about 40 in whom the disease has been recognized. It is probable, however, that many patients have recovered without diagnosis. Wetting of the bale before shredding, use of filters, and adequate ventilation have been effective protective measures. After removal from the contaminated atmosphere, the severely ill patient may be benefited by administration of oxygen and other supportive and palliative measures.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

60:597-652 (Dec.) 1952

Advances in Management of Acute Craniocerebral Injury. J. Raaf.—p. 597.
Report on 21 Cases of Nonspecific Ulcerative Terminal Ileitis. Y. Kim and B. Kim.—p. 606.
Lipoma of Uterus: Report of Three Cases. E. Henriksen.—p. 609.
Arthroplasty Versus Arthrodesis. B. Howorth.—p. 613.
Surgical Conditions of Male Breast. W. W. Greene.—p. 618.
Prolonged Pregnancy and Its Consequences. A. Temesvary.—p. 627.
*Chronic Poisoning of Endocrine Glands of Female Albino Mice by Cigarette Smoke. J. M. Essenberg.—p. 635.

The Endocrine Glands of Mice Following Inhalation of Cigarette Smoke.—In an earlier publication Essenberg and coworkers had demonstrated that cigarette smoke damaged the ovaries of mice. This report is concerned with the effect the inhalation of cigarette smoke has on the major glands of internal secretion as revealed by studies on the endocrine glands of 36 experimental and 24 control animals. The chamber of the smoking machine in which the mice were housed was automatically filled with the smoke of one cigarette every hour for 12 hours daily except Sunday. On the average, three to four minutes were required to burn the cigarette. The chamber was filled with smoke for about eight minutes. The smoke was almost gone in nine minutes. The tobacco smoke inhaled by the mice was approximately equivalent to the smoking of one package of cigarettes per day by human subjects. Exposure to the cigarette smoke was continued for 14 months. In the thyroids and in the suprarenal cortices, the damage consisted of cellular atrophy and hyalin degeneration. The less severe changes in the pancreas consisted of decrease in the number of islands of Langerhans and atrophy of pancreatic acini. No pathological changes could be demonstrated by histological techniques in the pituitary and parathyroids, but the effect on reproduction and on the growth rate indicates functional damage to the anterior pituitary. Nicotine is considered to be the major damaging agent.

West Virginia Medical Journal, Charleston

49:1-50 (Jan.) 1953

The Coronary Problem. A. McMahon.—p. 1.
Urologic Problems in Children. T. R. Fetter.—p. 12.
Present and Future Status of Medicine. L. H. Bauer.—p. 17.
Partial and Complete Pelvic Exenteration for Advanced and Recurrent Cancer. A. Brunschwig.—p. 21.

FOREIGN

Canadian Journal of Medical Sciences, Ottawa

30:443-594 (Dec.) 1952. **Partial Index**

Protein-Bound Phosphorus Compounds in Proximal Stump of Peripheral Nerve After Nerve Section or After Nerve Crush. J. E. Logan.—p. 457.
Lipid Composition and Water Content of Carcass, Skeletal Muscle, and Testicle in Host Component of Albino Rat—Walker Carcinoma 256 Dual Organism. E. M. Boyd, M. L. Connell and H. D. McEwen.—p. 471.
Nucleic Acids and Other Protein-Bound Phosphorus Compounds of Cat Brain: Incorporation of P^{32} After an Intracisternal Injection. K. P. Strickland.—p. 484.
Changes in Oxygen Uptake and Peptidase Activity of Rat Thymus During Growth and After Adrenalectomy. M. K. Birmingham and M.-L. Desbarats.—p. 494.
*Salmonella Typhosa Vi Antigen and Its Immunizing Potential. N. N. Swabb and G. B. Reed.—p. 503.
*Preliminary Comparative Study of Test Antigens Prepared from Adult and Larval Forms of Trichinella Spiralis. W. M. Ross.—p. 534.
Photometric Studies on Diazo Reaction for Serum Bilirubin. F. D. White and D. Duncan.—p. 552.
Immediate Effects of Severe Local X Irradiation on Liver of Hamster. K. E. Livingstone and D. J. McCallion.—p. 571.
Role of Adrenal Gland in Sodium Retention Following Acute Venous Obstruction. S. M. Friedman, M. Nakashima and C. L. Friedman. —p. 585.

Immunizing Potential of Salmonella Typhosa Vi Antigen.—Swabb and Reed found that cultures of typhoid bacilli containing Vi antigen were much more virulent for mice than strains in which the Vi antigen was not present. Vaccines prepared from all the Vi strains tested produced a much higher level of active immunity than vaccines prepared from W types lacking the Vi antigen. Serums of rabbits immunized with vaccines made from Vi strains produced a much higher level of passive immunity in mice than serums of rabbits immunized with non-Vi strains. The Vi antigen contained in vaccines prepared from certain strains, and one in particular, the Vi I vaccine of S. typhosa, proved to have greater thermostability and greater general stability, as tested by storage, than the Vi antigen of other strains. An acid extract of a Vi strain produced a high level of active immunity in mice.

Antigens from Adult and Larval Forms of Trichinella Spiralis.—Test antigens prepared respectively from adult and from larval forms of trichina were compared by means of the complement fixation test on serum from rabbits infected experimentally with varying numbers of trichinae. It had been hoped that by using an "adult" test antigen significant serum reactivity could be detected earlier during the course of infection than with the usual "larval" antigen. Although significant levels of reactivity were shown to occur with "adult" antigen, this form of antigen had no apparent advantage over the larval form of antigen in the detection of antibodies during early stages of trichinosis.

Clinical Science, London

2:315-462 (Nov.) 1952. **Partial Index**

Basis of Erythrocyte Sedimentation Rate. J. Hardwicke and J. R. Squire. —p. 333.
Renal Response to Respiratory Alkalosis. S. W. Stanbury and A. E. Thomson.—p. 357.
Some Evidence in Favour of Secretion of Water and Solutes by the Kidney. M. H. Roscoe.—p. 375.
Effects of Methyl Testosterone and Deoxycortone on Electrolytes. P. Fourman.—p. 387.
*Experimental Potassium Depletion in Man. D. A. K. Black and M. D. Milne.—p. 397.
Hypoferraemia in Human Subject: Importance of Diurnal Hypoferraemia. J. C. S. Paterson, D. Marrack and H. S. Wiggins.—p. 417.
Utilisation of Folic Acid from Natural Sources. G. H. Spray.—p. 425.
Iodine Uptake of Human Thyroid Throughout Menstrual Cycle and in Pregnancy. E. E. Pochin.—p. 441.
Secretion of Radioiodine in Digestive Juices and Milk in Man. A. J. Honour, N. B. Myant and E. N. Rowlands.—p. 447.

Experimental Potassium Depletion.—Evidence of potassium depletion has been found in a number of clinical syndromes, including gastroenteritis, diabetic coma, and Cushing's syndrome. Often the clinical situation is complicated by other metabolic abnormalities, which make it difficult to decide which symptoms are associated with the potassium depletion and which are due to other causes. In clinical states of potassium depletion, the severity of the depletion is usually assessed by noting the amount of potassium retained during recovery. To ascertain how far potassium retention can be relied on to indicate the magnitude of a known preexisting deficit, potassium depletion was produced in two normal men by a diet adequate in protein, calories and salt but containing less than 10 mEq. per day of potassium. Cumulative potassium deficits of 268 and 289 mEq. were attained. The corresponding retentions of potassium in the after-periods were 415 and 348 mEq.; these amounts are comparable to those found in acute clinical potassium depletion. Serum potassium levels fell to 3.1 and 2.6 mEq. per liter. The serum bicarbonate level rose, and in equilibrium states there was a negative correlation between the serum potassium and bicarbonate. The urinary pH rose, and the output of acid in the urine declined. There was retention of sodium and expansion of extracellular fluid, with an equivalent shrinkage of intracellular fluid. The calcium and magnesium balance was maintained. There was a negative phosphorus balance, but the loss of phosphorus was not equivalent to that of potassium. Nitrogen loss was not equivalent to that of potassium. The potassium deficit was negatively correlated with the rate of potassium excretion and the rise in serum potassium level after oral administration of potassium. Reasons are given for the view that extracellular alkalosis is caused by a shift of hydrogen ions into the cells, which modifies the valency of intracellular anion and preserves electroneutrality in spite of potassium loss. The absence of dramatic clinical symptoms in the subjects studied is attributed to the fact that adaptation to potassium depletion was not interfered with by other metabolic lesions; the adaptation that produces extracellular alkalosis may be important in preventing muscular weakness.

Deutsche medizinische Wochenschrift, Stuttgart

77:1591-1622 (Dec. 19) 1952. **Partial Index**

Experimental Foundations for Combined Use of Sulfonamides and Penicillin. G. Domagk.—p. 1591.
*Treatment of Uremia by Irrigation of Small Intestine. G. A. Martini. —p. 1595.
Corticotropin (ACTH) in Treatment of Schoenlein-Henoch Purpura. E. Buchborn.—p. 1598.
*Examination of Menstrual Blood in Genital Tuberculosis. H. Kräubig. —p. 1600.
Sympathetic Depressions. G. Dichgans.—p. 1602.
Weather and the Number of Births. R. Reiter.—p. 1605.

Treatment of Uremia by Irrigation of Small Intestine.—The artificial kidney, peritoneal irrigation, and gastric or intestinal irrigations are measures designed to bridge a critical period in cases of lower nephron nephrosis resulting from intravascular hemolysis, the crush syndrome, or toxicity caused by sulfonamides, heavy metals, or alcohol. The measures may also be used in patients with anuria following glomerulonephritis or the hepatorenal syndrome. Martini presents the histories of three patients in whom he resorted to irrigation of the small intestine. One patient, whose right kidney had been removed some years before, had preuremia following overindulgence in alcohol; another patient had the hepatorenal syndrome; and the third patient, who was subject to urolithiasis, had complete anuria following treatment with a sulfonamide. The irrigation of the small intestine was carried out as follows: A Miller-Abbott tube was passed down to the middle portion of the ileum and the rubber balloon near its distal end was inflated to block the intestinal lumen. The irrigation fluid was then introduced into the duodenum through an ordinary duodenal tube and suctioned off when it reached the distal end of the Miller-Abbott tube. The author irrrigated with Kolff's solution, which contains sodium chloride, sodium bicarbonate, potassium chloride, dextrose, calcium chloride, and magnesium sulfate. Since the rather high sodium chloride content of this solution may induce edema, Twiss reduced the sodium chloride content. The solution is introduced at body temperature. Suctioning off is done either by means of a syringe or by a suction device. Martini generally used 6 to 8 liters of fluid over a period of eight hours, but in some cases as much as 15 or 20 liters have been used. Since the irrigation may have to be

continued for 14 days, providing the patient with calories becomes important. The author now usually irrigates during the day, and introduces Bull's nutrient solution through the duodenal tube at night. This solution contains glucose, olive oil, and acacia. In the three cases described here, this method of irrigation of the small intestine effected rapid improvement in the uremia.

Examination of Menstrual Blood in Genital Tuberculosis.—The diagnosis of genital tuberculosis is often difficult. The history, pelvic examination, tuberculin test, complement fixation reaction, and blood picture provide only presumptive evidence of the disease. On the other hand, surgical diagnostic measures such as exploratory laparotomy or curettage are dangerous, in that they have been known to result in formation of a fistula, in miliary dissemination, and even in death. An additional diagnostic technique described by Kirchhoff is the examination of menstrual blood for tubercle bacilli, preferably a specimen collected by an occlusive pessary at the onset of the flow. These are identified by Ziehl-Neelsen staining, culturing, or animal inoculation. In studies performed by Kräubig, Ziehl-Neelsen staining never gave positive results, and cultures produced few positive results. Animal inoculation of menstrual blood proved more effective and has been used in 253 cases. So far 69 positive results have been obtained by this method. In 32 histologically verified cases of genital tuberculosis, 19 were proved positive by animal inoculation with menstrual blood. Since diagnosis by animal inoculation requires from six to eight weeks, a more rapid technique was investigated. The menstrual blood was examined for tubercle bacilli by means of fluorescence microscopy. Of 61 specimens of menstrual blood in which both fluorescence microscopy and animal inoculation were employed, the results of the two methods were identical in 29 cases. In 24 specimens negative on fluorescence microscopy, the animal inoculation later gave positive results; whereas in 8 cases with specimens positive on fluorescence microscopy, the results of animal inoculation were negative. The author feels that animal inoculation is more reliable and that a definite diagnosis cannot be based on the results of fluorescence microscopy alone. Examination of the menstrual blood for tubercle bacilli is helpful not only in diagnosis but also in estimating the results of treatment, curettage being too dangerous a method for this purpose.

Die Medizinische, Stuttgart

No. 50:1585-1616 (Dec. 13) 1952

Schizophrenia. H. W. Gruhle.—p. 1585.
*Limitations of Morphologic Diagnosis of Carcinoma of the Uterine Cervix. H. Cramer.—p. 1589.
Anti-inflammatory Effect of Cortisone, Corticotropin, Pyrazolone and Other Antiphlogistic Substances. G. Wilhelmi.—p. 1591.
Is Local and Intraperitoneal Administration of Sulfonamide Still Justified in Gynecology and Obstetrics? C. Dolff.—p. 1596.
Corticotropin in Symptomatic Treatment of Lipoid Nephrosis: Case Report. J. Scholten and G. Schulz.—p. 1600.

Limits of Morphological Diagnosis of Carcinoma of Cervix.—It is generally accepted that the presence of an infiltrating growth establishes the diagnosis of carcinoma of the cervix, but in cases in which infiltration and destruction are still absent, the diagnosis largely depends on the evaluation of atypical features of the epithelium in the form of anaplasia, polymorphism, hyper- and polychromasia, and abundance of mitoses and in a displacing, invading growth deep into the cervical glands. In this stage most pathologists employ the concept of the preinvasive, superficial, or intraepithelial carcinoma, the so-called carcinoma in situ. This cytomorphological diagnosis is based chiefly on the fact that, at this stage, atypical features are found that are also present in infiltrating carcinoma. Since regressions have been observed at this stage, this is not a sufficient basis for diagnosis of carcinoma. Assuming that anaplasia, atypia, and polymorphism of the nuclei would permit standardization of nuclear size and variations in size, Cramer measured the sizes of nuclei in specimens from normal cervices and from those with atypical features. Most other investigators had been content with the comparison of average values and had dispensed with exact statistical evaluation. Cramer found that when in atypical cervical epithelium sizes of nuclei and fluctuations in nuclear magnitudes occur that resemble those of normal basilar or prickle cells, this cannot be regarded as an indication of incipient intraepithelial carcinomatous change but neither can it definitely rule out the carcinomatous nature of this atypia. On the other hand, nuclear sizes in excess of 120 surface units (the product of longitudinal and transverse diameters) are highly suspicious, and those in excess of 180 surface units may be regarded as proof of the carcinomatous nature of an atypical epithelium, particularly if such excessive sizes are accompanied by irregular nuclear variations. The author is convinced that large nuclei with a great range of scatter, when they can be demonstrated in large groups of about 100 nuclei, can be regarded as corroborative evidence for the carcinomatous nature of a surface layer.

Gazzetta Medica Italiana, Milan

111:253-284 (Oct.) 1952. Partial Index

*Erythropoietic Action of Cobalt Glutamate. D. Castelli and L. Varetto.—p. 253.
Hemostatic Action of Thrombin: Experimental Studies. L. Enrico.—p. 261.
Rectal Administration of Sulfonamides in Treatment of Children. E. Grasso and B. Fantuzzi.—p. 264.

Cobalt and Erythropoiesis.—Cobalt glutamate was given to 20 guinea pigs in which anemia had been induced by withdrawing 10 to 15 cc. of blood from the heart. It had a definite erythropoietic action and influenced hemoglobin synthesis. Two animals received intramuscularly 40 mg. of the drug per kilogram of body weight, two received 50 mg., eight received 3 mg., and eight received 6 mg. Six additional animals were bled and served as controls. In the four animals that were given large doses of cobalt glutamate, the reticulocytes increased greatly and this increase persisted much longer than that observed in the controls. The initial values of hemoglobin and erythrocytes were also reached sooner than in the controls, and there was an increase in the hemoglobin level of from 5 to 23% above the initial level and in the erythrocytes of about 14.5%. The maturation of the red cell series of the bone marrow was accelerated, and there was prevalance of polychromatophils. In the animals treated with 3 or 6 mg. of the drug per kilogram of body weight, the reticulocytes increased and this increase persisted as long as 20 to 30 days. After the initial values of hemoglobin and erythrocytes were reached, there was an increase of 27.8% in the hemoglobin and of 32.5% in the erythrocytes of those that received 6 mg. of the drug per kilogram of body weight and of 13.1% in the hemoglobin and 13.3% in the erythrocytes of those treated with 3 mg. of the drug per kilogram of body weight. The so-called cobalt-induced polycythemia was present in all the animals. It was a polycythemia vera, since the number of reticulocytes was always increased, and on the 15th and 16th day of treatment the curve of erythroblastic maturation showed an acceleration even in the animals that had signs of intoxication. In fact, the doses of 40 or 50 mg. per kilogram of body weight proved too large, and after 12 to 14 days of euphoria toxic signs began to appear and all the animals were dead by the 18th day. Autopsy revealed congestion of recent onset in the kidneys, lungs, and liver. Only two of the other animals died, on the 20th and 30th days respectively; the others and the controls were killed. In these there were no signs of microscopic alterations to the organs, although there were signs of mild vacuolar degeneration of the liver in the animals that received the small doses of cobalt glutamate.

Journal of Laryngology and Otology, London

66:583-634 (Dec.) 1952

Course of Nasal Airstreams. J. D. K. Dawes.—p. 583.
Hearing of Patients After Tuberculous Meningitis. A. S. Walker.—p. 594.
Management of Bilateral Paralysis of Vocal Cords Following Operations on or Diseases of Thyroid Gland. J. A. Harpman.—p. 599.
Comparison of Physical Characteristics of Five Well-Known Hearing-Aids With Theoretical and Apparent Subjective Needs of Patient. J. J. Groen and J. W. Tappin.—p. 604.

Lancet, London

2:1189-1234 (Dec. 20) 1952

Afferent-Loop Syndrome: Bilious Regurgitation After Subtotal Gastrectomy and Its Relief. C. A. Wells and I. W. MacPhee.—p. 1189.
*Healing Polyarteritis Nodosa: Observations on Three Cases After A.C.T.H. and on One Case After Sympathectomy. W. St. C. Symmers and J. A. Litchfield.—p. 1193.
Fatal Appendicitis: Decline in Mortality. W. S. Rees.—p. 1199.
Congenital Absence of Common Bile-Duct. H. L. Durell and A. C. Halliwell.—p. 1203.
Treatment of Pneumococcal Meningitis Since Introduction of Penicillin. D. Gibson and D. G. James.—p. 1203.
Gown for Incontinent Patients. A. Arnott and N. H. Nisbet.—p. 1206.

Healing of Polyarteritis Nodosa After Treatment with Corticotropin and Sympathectomy.—Four cases of polyarteritis nodosa are reported in which all the arteritic lesions showed advanced or complete healing. Two of the three patients treated with corticotropin died of complications of the disease, which were unavoidable in one case and possibly due to arterial hypertension in the other; the treatment may have caused the death of the third patient. These three cases are important because histological studies post mortem revealed evidence of the remarkable extent to which the lesions of polyarteritis nodosa may heal by fibrosis under the influence of corticotropin. The paradoxical association of healing of the lesions and death is not remarkable in a disease that threatens every organ with the consequences of vascular occlusion. In many cases the lesions must already be widely disseminated by the time the diagnosis is made, and often the vasculature of the vital organs will have been so damaged that no treatment will save the patient from disablement or death. The possibily disastrous effects of obliterative healing of affected vessels in organs such as the heart and kidneys do not constitute a contraindication to treatment; the same effects might as readily develop if the patient survived long enough for healing to take place naturally. At the present time the authors are observing cases of histologically confirmed polyarteritis nodosa in which there is no evidence of disease a year or more after treatment with corticotropin. Such cases, however uncertain their ultimate outcome, are a further encouragement to persevere with this treatment. In the fourth patient described here, the lesions healed after sympathectomy for malignant hypertension. The authors feel that, if lowering the blood pressure in hypertensive patients with polyarteritis nodosa can cause healing of the arteritic lesions, better therapeutic results may possibly be obtained with corticotropin or with cortisone if the hormone therapy is supplemented in such cases by antihypertensive treatment with drugs or by surgery.

Medical Journal of Australia, Sydney

2:729-760 (Nov. 22) 1952

Psychiatry, the State, and the Individual. B. Mulvany.—p. 729.
*Occurrence of Secondary Malignant Disease in Spleen. G. W. Milton.—p. 736.
Scope of Modern Industrial Medicine. A. L. Langley.—p. 740.
Intraabdominal Use of Penicillin. F. H. Shaw and G. T. Peterson.—p. 742.
Five Cases of Paralytic Poliomyelitis in a Family. B. P. McCloskey.—p. 744.
Dextran in Blackwater Fever. C. E. M. Gunther and H. B. Bruce.—p. 745.

Malignant Disease of Spleen.—After citing earlier reports providing evidence that the spleen is an unusual site for metastatic cancer, Milton reports on a series of 3,620 autopsies in which microscopic examination of the spleen was carried out. In 653 autopsies cancer was found in some part of the body, and in 25 of these there were secondary deposits in the spleen. The theories devised to explain the rarity of secondary deposits in the spleen have been based on the mechanics of the splenic circulation or the production of some unknown growth-inhibiting substance. Milton, however, feels that anatomic factors may explain, at least in part, the lack or rarity of splenic metastases. The strong fibromuscular capsule would offer a barrier to direct penetration. Lymphatic spread to the spleen is hampered by the poorly developed lymph vessels. The spleen has no afferent lymphatics that drain from an organ in which malignant disease is common. Malignant permeation of lymph vessels must, therefore, be retrograde against the flow of lymph before it can reach the pulp, but retrograde flow is not common. Since there is little mixing of blood in the portal vein, it is unlikely that malignant cells would be regurgitated into the spleen. This leaves the splenic artery as the most likely route for conveyance of malignant emboli to the spleen. This concept was supported by the observation that clumps of cancer cells were found only in the red pulp. All carcinomas involving the spleen had access to the arterial circulation, as was shown by the frequency of deposits in the lungs and in sites that were at some distance from the primary growth, such as bones. Discrete secondary deposits in the spleen in any case of malignant disease indicate a bad prognosis, splenic deposits occurring only in those cases in which widespread arterial-borne metastases have appeared. There is no clinical method of diagnosing secondary malignant disease in the spleen.

Minerva Chirurgica, Turin

7:757-798 (Oct. 31) 1952. **Partial Index**

*Clinical and Experimental Study of Renal Function After Ligation of Inferior Vena Cava. O. Mantero, G. Barlassina and G. Monteverde.—p. 757.
*Application of Filatov's Therapy in Surgery. M. Ferrando and L. Cibrario.—p. 767.
Anatomicosurgical Studies of Segmental Pulmonary Resection. N. Berri and L. Enrico.—p. 771.

Renal Function After Ligation of Inferior Vena Cava.—The inferior vena cava was ligated in seven normal dogs and in three patients with heart disease, and a comparative study was made to prove whether the clinical improvement brought about by this operation in patients with heart disease is attributable to changes in the renal circulation. In the animals the abrupt disturbance in the venous circulation caused by the ligation had unfavorable effects on the heart: the amount of blood going to the right heart diminished, the pressure within the right ventricle dropped, causing a proportional drop in the output of both ventricles and therefore diminished blood flow to the kidneys as the direct consequence of a weaker left systole. In fact, the glomerular filtration rate, the renal plasma flow, and the blood supply to the kidneys diminished in all the animals. Only the maximum rate of tubular excretion remained normal, and this shows that the operation does not alter the specific function of the tubular epithelium and that the changes in the clearances values are due to vascular imbalances only. Two of the patients (34 and 38 years old) had congestive heart failure of four years' and five to six months' duration respectively; the other, a 51-year-old woman, had a mitral aortic lesion with left heart insufficiency of five to six months' standing. All had auricular flutter-fibrillation arrhythmia and in all the etiological factor was a previous rheumatic infection. Two to five months after the ligation, their general condition and the condition of the heart and the circulation were satisfactory. They could leave the bed for several hours every day and perform some housework that preoperatively had been impossible. The renal function in these patients was studied 26, 16, and 30 days, respectively, after the operation. Results in the first two patients differed substantially from those in the third. In the former the glomerular filtration rate, the renal plasma flow, and the blood supply to the kidneys increased, the arteriolar resistance of the nephron decreased, and diuresis increased. These patients were operated on in a period of right heart overload and had the maximum benefit from the ligation, with a consequent increase in circulatory efficiency and in blood supply to the kidneys. In the third patient the ligation caused a diminution of both right and left ventricular output, resulting in regression of the pulmonary stasis and a decreased flow of arterial blood to the kidneys. The effects on renal function were the same as those obtained in the dogs. The clinical improvement in this patient is attributable only to the improved hemodynamic condition of the right heart and the pulmonary circulation as a result of the constant decrease in their pressures following the operation. On the basis of these data the authors conclude that ligation of the inferior vena cava is indicated for patients with congestive heart failure and mainly for those in whom this is associated with lesions of the valves.

Filatov's Therapy in Surgery.—Treatment with injections of aqueous placental extract or placental emulsions, or with grafts of placental tissue is based on Filatov's theory that certain elements called "biogenous stimulators" are present in the cells of tissues in a particular phase of their life preceding death. These stimulators were found in fragments of placenta, and if the fragments were preserved at 3 to 4 C for three to four days, they became more numerous. In this paper the authors report the good results obtained with this therapy in nine patients. One patient, a heavy smoker with Buerger's disease, had gangrene in the first two toes of the left foot and had been referred to the authors for amputation. After 50 injections (one daily) of aqueous placental extract, four injections of placental emulsion (one every two weeks), and two implantations of placental and one of amniotic tissue under the skin of the abdomen, the two toes became detached, the wounds showed a pink granulation, and pain began to disappear. Three months later sweat could be seen on the leg, the color of the skin was normal, and there were no signs of cyanosis. In one diabetic with plantar ulcerations of both feet and an intense fetid secretion, epithelization and delimitation of the necrotic process was obtained with one placental graft and simultaneous injections of aqueous placental extract, while at the same time the diet and insulin administration were checked carefully. Acceleration of the processes of cicatrization and improvement in the nutrition of the tissues was obtained in four patients who had open wounds of traumatic origin in the lower extremities. These were of recent origin in two of the patients, and of 30 and 2 years' duration, respectively, in the other two. Two patients, a 70-year-old woman and a 65-year-old man, had varicose ulcers with serous secretion and a pronounced eczematous reaction of the surrounding skin. After 40 injections (one daily) of aqueous placental extract their general condition improved, the size of the ulcers and the amount of secretion decreased, the eczematous reaction disappeared, epithelization occurred, and the patients recovered. This therapy was also attempted in a woman with rheumatic polyarthritis and chronic arthrosis of the left shoulder in whom the movements of abduction and circumduction of the humerus were restricted and in whom all medical therapy had failed. After two daily injections of aqueous placental extract for 15 days, two injections of placental emulsion (one every eight days), and one implantation of a desiccated placental graft, she was able to perform some of these movements with ease, although the function of the shoulder was never restored entirely. Allergic reactions or other side-effects did not occur in any patient during the treatment. There was only soreness in the extremities and in the area where the injections, especially of placental emulsion, were given.

Practitioner, London

169:585-694 (Dec.) 1952. **Partial Index**

Newer Antibiotics in Respiratory Infections. T. Anderson.—p. 589.
Care of the Chronic Asthmatic. E. M. Buzzard.—p. 596.
Bronchiectasis and Its Treatment. N. Oswald.—p. 605.
Emphysema. B. O'Brien.—p. 613.
The Problem of the Child with Chronic Cough.. A. D. Bell.—p. 620.
Prevention of Respiratory Infection in a Closed Community. T. A. A. Hunter. —p. 628.
Colds as a Diagnostic Problem. M. C. Cheney.—p. 633.
Dupuytren's Contracture. D. N. Matthews.—p. 641.

Presse Médicale, Paris

60:1547-1566 (Nov. 15) 1952. **Partial Index**

Crystallized Thevetia Neriifolia Extract in Treatment of Cardiac Decompensation. C. Lian.—p. 1547.
Necessity and Possibility of Preventing Undesirable Pleural Side-Effects After Section of Adhesions in Artificial Pneumothorax. F. Triboulet and T. Liokis.—p. 1548.
Muscle Pain In Course and Decline of Sciatica Due to Herniated Disk. J. N. Taptas.—p. 1549.
*Treatment of Periarthritis of Shoulder by Local Application of Ice. P. Ducroquet and B. Jaulmes.—p. 1553.

Local Application of Ice in Periarthritis of Shoulder.—Fixation of the shoulder joint with an abduction splint or an amply fenestrated thoracicohumeral plaster of paris cast combined with continued local application of ice has proved to be the treatment of choice for acute ankylosing periarthritis of the shoulder with or without calcifications and for simple hyperalgesic periarthritis of the shoulder. A rubber bag filled with unsalted ice fully covers the cutaneous surface corresponding to the external and upper anterior surface of the shoulder joint. The ice should be renewed every three to four hours, a piece of cloth placed between the ice bag and the skin. Pain decreases rapidly, and in general subsides completely within 48 hours. Mobilization may be started on the third or fourth day, but fixation and application of ice is discontinued only during the mobilization intervals and should be maintained for at least 8 to 10 days. Local application of ice alone without fixation is to be considered adequate only for cases of simple periarthritis associated with moderate pain. While treatment with analgesics proved to be only palliative and use of procaine as well as physical therapy is associated with the risk of secondary exacerbation of pain, local application of ice has the advantages of simple application, being harmless and rapidly effective. Roentgenological examination revealed disappearance within 8 to 10 days of calcifications in the subdeltoid bursa or in the tendon of the supinator muscle. While cortisone may act rapidly and effectively on pain, it exerts only a very limited effect on the mobility; it often requires hospitalization and is expensive. It seems therefore logical to give application of ice a trial even in refractory cases before cortisone therapy is instituted. Local application of ice may also be a valuable adjuvant to surgical treatment (acromiectomy) in ankylosing and fixed forms of periarthritis of the shoulder. The authors believe that the mechanism of their method of treatment consists of a reflex action, with the skin as the starting point. According to Hilton's law, there is anatomic and physiological correspondence between the articular, muscular, and cutaneous innervation. The cold by its action on vessels and nerves combats local hyperemia, periarticular inflammation, and deep capsular edema.

60:1599-1618 (Nov. 22) 1952

*Conservative Surgical Treatment of Arteritis of Lower Extremities (Sympathectomy, Adrenalectomy): Results of Interventions Performed in Course of Four Years. J. Ducuing, A. Enjalbert, A. Gédéon and R. Bruguier.—p. 1599.
Is Asthma a "Disease of Adaptation"? (Answer to Professor H. Selye.) J. Turiaf.—p. 1601.
BCG Vaccination of 82 Persons in Familial Tuberculous Environment and Not Separated From Source of Contagion. M. Fourestier, A. Blacque-Belair and R. Robert.—p. 1602.

Conservative Surgical Treatment of Arteritis.—Between 1947 and 1950, 89 patients with arteritis of the lower extremities were subjected to arteriography and conservative surgical treatment. Of these 89 patients, 65 had arteriosclerotic arteritis, for which the term "arteritis due to overload (surcharge)" was coined by Leriche. This type of arteritis occurs most frequently in patients over 50. Patients with this type of arteritis were treated by indirect methods for increasing blood flow such as lumbar sympathectomy, or arteriectomy in cases of thrombotic arteries, or of both these interventions combined except in cases of segmental thrombosis when direct methods of treatment such as venous autografts or preserved arterial homografts were used. There were six operative deaths in this group, and eight patients were lost to observation. Of the remaining 51, 11 died postoperatively, 4 became worse as a result of the intervention, 27 obtained excellent results with pronounced functional improvement, 7 were moderately improved, and 2 had unsatisfactory results requiring secondary amputation. The large number of deaths occurring relatively early in the postoperative course suggests an unfavorable prognosis in arteritis due to overload; it depends on the degree of vascularity of the heart and the brain. The remaining 24 of the 89 patients were less than 40 years old and had thromboangiitis; 20 of these patients were treated by total left adrenalectomy followed in a second stage by right splanchnicectomy, 1 patient underwent total left adrenalectomy and in a second stage partial right adrenalectomy, 2 had total right adrenalectomies, and 1 total left adrenalectomy. The last mentioned patient died in shock the night after the intervention, and necropsy re-

vealed a large hematoma in the renal fossa; it was the only fatal case in this group of 24 patients, 3 of whom were lost to observation. One patient had postoperative hemiplegia, 11 obtained satisfactory results and 5 moderate results. Three were therapeutic failures, presenting a malignant syndrome with the early postoperative appearance of gangrenous lesions or painful vasomotor disturbances requiring amputation; new distal thromboses may occur and the electrocardiogram, which up to then may have been normal, may show coronary involvement. The late prognosis of surgically treated thromboangiitis seems to be more favorable than that of arteritis due to overload. Whatever the type of arteritis for which the patient undergoes conservative surgical treatment, he enters a new phase of his disease, which may regress, remain stationary, or progress after a latent period of various duration.

Quarterly Journal of Medicine, Oxford

21:361-464 (Oct.) 1952

Haemodynamic Basis of Symptoms and Signs in Mitral Valvular Disease. G. Wade, L. Werkö, H. Eliasch and others.—p. 361.
Factors in Aetiology of Diabetic Glomerulosclerosis. G. F. M. Hall. —p. 385.
Articular and Other Limb Changes in Acromegaly: Clinical and Pathological Study of 25 Cases. J. H. Kellgren, J. Ball and G. K. Tutton. —p. 405.
Metabolic Disorder in Hepato-Lenticular Degeneration. W. B. Matthews, M. D. Milne and M. Bell.—p. 425.
Maintenance and Completion of Artificial Pneumothorax: Study of 315 Completed Cases. W. C. Harris, F. C. Poles and A. W. Anderson. —p. 447.

Semaine des Hôpitaux de Paris

28:3605-3642 (Dec. 2) 1952

National and International Problems of Mass Medicine. Six Years' Experience with Application of Ordinance of November 2, 1945 Concerning Services for Maternal and Infantile Protection. E. Aujaleu and O. Lacambre.—p. 3605.
Medical Secret with Respect to Social Security Law. C. Berlioz.—p. 3610.
*Vaccination and Revaccination With BCG.-S. (BCG-Recall). L. H. Lafay-Coletsos, S. Dauvé-Collardeau and J. Deligné.—p. 3614.

Vaccination and Revaccination with BCG.—In 1948, debilitated children recovering from epidemic diseases or surgical interventions were admitted to a convalescent home on the coast of Normandy, France, for a three month rest period. On admission they were given a tuberculin scarification test and the parents' consent was asked for BCG vaccination of children who had negative results from the test. After a sojourn of two months in the home, BCG vaccination was administered. Postvaccinal allergy resulted within one month in 92.1% of the 704 vaccinated children, within two months in 94.2%, and within three months in 96%. The allergy was detected by the tuberculin scarification reaction in 56.2%, by the intracutaneous reaction to 50 I. U. in 39.2%, and by Vollmer's patch test in 4.5% of the cases. Up to 1951 not a single case of tuberculosis was detected among the BCG-vaccinated children. In November, 1951, a BCG vaccination center was established in Paris in a dispensary from which tuberculous patients were barred. Of 720 BCG-vaccinated children who were invited by the center for follow-up examination, 503 submitted to Vollmer's patch test and 403 of them had positive results from the test, while the remaining 100 who had negative results were given a BCG test, i. e., the skin was scarified through one drop of fresh BCG vaccine. Within 1 to 16 days the reaction to the BCG test became positive in 97. Of the 503 children previously vaccinated with BCG, 100 had been vaccinated one year ago and 107 two years ago. Of the 100 children, 71 had positive results from the tuberculin patch test while the remaining 29 had negative results and their reactions to the BCG test became positive within 2 to 10 days. Of the 107 children, 77 had positive results from the tuberculin patch test, while the remaining 30 had negative results and their reactions to the BCG test became positive within 1 to 12 days. These data provide objective proof of the extreme sensitivity of the skin to the BCG test. In 95% of the children vaccinated previously with BCG who were given the BCG test the reaction to the test became positive within five days; it seems logical to admit that in these children the BCG test acted as vaccination with a recall dose that may be adequate to consolidate a still considerable allergy. Children in whom the reaction to the BCG test becomes positive between the 10th and 16th day should be given a tuberculin patch test three months after they had been given the BCG recall dose; if they have a negative result from the tuberculin patch test, they should be given a repeated recall dose of BCG. The BCG scarification test is more reliable than any other procedure in detecting an allergy that is declining with years and in securing simultaneously a minimal revaccination for which the term "BCG-recall" is suggested.

28:3689-3726 (Dec. 10) 1952. **Partial Index**

Epilepsy due to Cardiovascular Affections. C. Lian and J. Welfling. —p. 3689.
*So-Called Endocarditis Lenta. W. Loeffler.—p. 3693.
*Importance of Muscular Biopsy in Clinical Diagnosis of So-called Collagen Diseases. V. Chini and G. Malaguzzi-Valéri.—p. 3699.
Surgical Treatment of Congenital Stenosis of Aortic Isthmus. P. Santy. —p. 3705.

Endocarditis Lenta.—The classic rheumatic and ulcerative forms of endocarditis are separated by several intermediate conditions, the best known being Osler's subacute bacterial endocarditis or endocarditis lenta. This condition can no longer be considered an etiological entity, because it may be caused by many different micro-organisms. It represents a stage in the development of a pathological process that was usually fatal before the advent of penicillin. Many forms of endocarditis with negative blood cultures seem to occupy a position between the subacute bacterial and the classic rheumatic types. Their duration is longer than that of the rheumatic type and they are highly refractory to antibiotic treatment as well as to salicylates. Antibiotic treatment, on the other hand, when started early enough is effective in subacute bacterial endocarditis. Penicillin, given in doses of from 500,000 to 900,000 units a day, will control the infection in 90% of the cases; massive doses, combined with other antibiotics, may occasionally be required. The refractory cases are chiefly those in which the causative organism cannot be identified. Constantly high levels and persistent abnormal groupings of plasma proteins indicate that the infection has not yet been conquered; treatment should be continued until disturbances of the plasma proteins have disappeared. Analysis of the results of antibiotic treatment shows that mechanical damage to the heart persists or even increases, although the patient may be bacteriologically cured. Generalized lesions of the capillary endothelium in subacute bacterial endocarditis constitute a strict contraindication to anticoagulant therapy. Cortisone and corticotropin are useful in cases bordering on rheumatic endocarditis, in which the virulence of the causative organism is weak and the systemic reaction is significant or even excessive. They are not indicated in subacute bacterial endocarditis; in the ulcerative forms, however, in which adrenal depletion exists (Waterhouse-Friderichsen syndrome), substitution therapy with cortisone (not corticotropin) is vital. Rheumatic endocarditis is an expression of high resistance to a weakly virulent agent, while ulcerative endocarditis shows low resistance to one that is highly virulent. Endocarditis lenta occupies an intermediate position, representing a kind of uncertain balance between the virulence of the micro-organisms and the resistance of the body. Certain atypical or abortive nonbacterial forms have a specifically calcifying tendency. Spontaneous recovery in these forms sometimes takes place, but even if the inflammatory process is arrested, the injury to the heart valves caused by cicatricial calcification may eventually result in death. Fatal cicatricial processes may also be found in cases of nonbacterial endocarditis of the Libman-Saks and Felty types, as well as Loeffler's parietal endocarditis.

Muscle Biopsy in Collagen Diseases.—Diagnosis of the so-called collagen diseases is sometimes very easy and sometimes extremely difficult. Many laboratory tests are inconclusive, and some may even be misleading, but muscle (calf) biopsy has proved uniformly valuable. The authors believe that malignant visceral lupus erythematosus, with or without cutaneous manifestations, Libman-Saks syndrome, with or without atypical verrucous endocarditis, and some types of so-called subacute

bacterial endocarditis with negative blood cultures are all clinical variants of a single large pathological group. Careful clinical, histological (muscle biopsy), and humoral studies were made on approximately 60 patients with rheumatic cardiovascular diseases. Obvious histological changes were present in the muscles, differing according to the disease type. These changes were chiefly of two kinds: vascular (found in nodular panarteritis) and parenchymal (found in malignant visceral lupus erythematosus). Differential diagnosis between these conditions is easy enough in extreme cases, but muscle biopsy may be the only means of establishing it in intermediate cases. Humoral and muscular changes similar to those of malignant lupus erythematosus may be found in cases without cutaneous manifestations (lupus sine lupo), for which the name "malignant visceritis" is suggested; the clinical course is the same in both. Subacute bacterial endocarditis with negative blood cultures is present in some of these cases. The greatest diagnostic difficulties are found in the rheumatic conditions, in which it is often hard to distinguish between severe bacterial endocarditis, a beginning subacute bacterial endocarditis, and "malignant visceritis" without cutaneous manifestations superimposed on bacterial endocarditis. Muscle biopsy shows that these conditions fall into two groups: (1) those without significant histological changes and (2) those with histological changes (sometimes severe) resembling the ones found in lupus erythematosus. Conditions in the first group are benefited by intensive antirheumatic treatment, while those in the second are not improved by salicylates, antibiotics, or corticotropin. The presence of histological changes in muscle, therefore, indicates a poor prognosis in bacterial endocarditis; such changes probably show that the conditions in which they are found are collagen diseases and should be classed as malignant visceritis rather than simple endocarditis. Certain focal infections also cause extensive histological changes in the muscles similar to those found in the collagen diseases; suppression of the foci may lead to clinical cure and improvement, but not complete regression, of the histological changes. Muscle biopsy is a valuable diagnostic aid, facilitating the choice of treatment and indicating the prognosis, and should be more widely used.

Ulster Medical Journal, Belfast

21:101-204 (Nov. 1) 1952. **Partial Index**

Cystic Disease of Lungs. R. J. Young.—p. 142.
Farmer's Lung: Clinical Account of Disease Probably Caused by Fungi. P. J. Sweeney.—p. 150.
*Hepatolenticular Degeneration (Wilson's Disease). C. G. Warnock.—p. 155.
Trochanteric Fracture of Femur. R. J. W. Withers.—p. 172.
Long-Stay Accommodation for Elderly Irremediable Patient. G. F. Adams.—p. 177.

Hepatolenticular Degeneration (Wilson's Disease).—Wilson's disease is a hereditary disorder characterized by cirrhosis of the liver and degenerative changes in the lenticular nuclei of the brain. The liver is affected long before nervous symptoms appear. During this "prodromal" phase portal hypertension with jaundice and ascites or splenomegaly with anemia and hemorrhagic phenomena may appear. Not infrequently, death occurs at this stage and the correct diagnosis only becomes apparent when another member of the same family shows the complete symptomatology. Liver disease may become quiescent before nervous disturbances appear; at any rate, hepatic damage is less prominent in the later phases of the disease. The classical features are those of extrapyramidal motor dysfunction, in the form of a coarse action tremor of the extremities together with a plastic muscular rigidity, leading to contractures. Dysarthria and dysphagia are prominent symptoms and a sustained grin or "spastic smile" is characteristic. Varying degrees of mental deterioration may be present. In this form of the disease the nervous symptoms appear in youth or adolescence, and death often occurs in a few months. In other patients the onset is much later in life, and the whole process is more gradual and prolonged. Here, the outstanding symptom is tremor, without difficulties of deglutition or articulation, at least until the later stages. Rigid facies like that seen in Parkinson's disease is common. Prior to Wilson's discovery of the disease, the condition was thought to be allied to multiple sclerosis, hence the term "pseudosclerosis." Still another variation of the syndrome is exemplified by cases in which torsion dystonia is a prominent neurological feature. There is, however, one pathognomonic sign that is common to all the aforementioned variants, and is present in about 80% of cases, namely, corneal pigment—the so-called "Kayser-Fleischer ring." The five cases described here by Warnock illustrate several of the clinical varieties. After discussing these cases, the author reviews the recent literature on this condition, pointing out that large quantities of copper can be recovered from liver and brain tissues at autopsy. This deposition constitutes a "biochemical lesion," which is potentially reversible, according to Denny-Brown and Porter. Copper is excreted in excessive quantities in the urine, and this output can be still further raised by administration of dimercaprol (BAL). The mobilization of copper, in response to dimercaprol, is followed by improvement in neurological symptoms and in liver dysfunction. Although relapses may occur, repeated courses of the drug can control the progress of the disease. It is believed, however, that this is more likely in the chronic ("pseudosclerosis") type than in the acutely progressive variety. A second metabolic peculiarity characteristic of the disease is aminoaciduria. It exists not only in fully developed cases with neurological symptoms, but also in the purely hepatic form, and even in siblings with no demonstrable abnormality either in liver or central nervous system. So far, the relationship between this anomaly and the derangement of copper metabolism has not been explained, but it is a constant association in these cases. The aminoaciduria is easily demonstrable by paper chromatography. These two chemical abnormalities provide a possibility of recognizing the disease much earlier than has previously been possible, and of detecting potential victims in families where known cases already exist. Treatment could then be given at a time when it is most likely to be beneficial.

Zeitschrift für Tuberkulose, Leipzig

101:113-272 (No. 3 & 4) 1952. **Partial Index**

Treatment of Tuberculous Diabetics with Special Considerations of Collapse Therapy. W. Jäpel.—p. 113.
Antibacterial Therapy of Tuberculous Empyema. W. Stahlmann.—p. 130.
Change in Position of Cavities During Thoracoplasty. A. Horn.—p. 151.
Course of Experimental Guinea Pig Tuberculosis Under Influence of Isonicotinic Acid Hydrazid. W. Finkeldey.—p. 166.
*Comparative Bacteriologic-Clinical Investigations on Resistance of Tubercle Bacilli to Antibiotics and Chemotherapeutics. J. Hein and H. Wemmers.—p. 170.

Resistance of Tubercle Bacilli to Antibiotics.—The tubercle bacilli in sputums of patients with tuberculosis were tested for their sensitivity or resistance to streptomycin, para-aminosalicylic acid and thiosemicarbazone (amithiozone); the results were then compared with the clinical and roentgenologic observations on these patients. A total of 337 resistance determinations were made on 218 patients. As regards treatment with streptomycin, there was a decided discrepancy between bacteriological, clinical, and roentgenologic observations; one-fourth of those who proved bacteriologically sensitive to streptomycin therapy derived no improvement, whereas a third of those who were resistant showed further retrogression of the lesions on continuation of streptomycin therapy. Consequently the authors feel that even with continuous tests at regular intervals, the outcome of bacteriological sensitivity tests is less decisive than the clinical picture. Since isoniazid was introduced into the chemotherapy of tuberculosis, this substance has also been tested as regards production of resistant strains of tubercle bacilli. It was found that resistance to this substance develops even more rapidly than to streptomycin, at least in some strains. The isoniazid content of various body fluids was determined with the method of Geks as well as with the procedure of Kelley and Poet. The values obtained with these two methods were either identical or were very close together. Apparently isoniazid is excreted largely through the kidneys, since urine always contained the highest concentrations. The virulence of tubercle bacilli that have become resistant is now being determined in animal experiments, and the concentration of isoniazid in the tissues is also being investigated.

BOOK REVIEWS

Psychiatry and the Law. By Manfred S. Guttmacher, Chief Medical Officer, Supreme Bench of Baltimore, Baltimore, and Henry Weihofen, Professor of Law, University of New Mexico, Albuquerque. Cloth. $7.50. Pp. 476. W. W. Norton & Company, Inc., 101 Fifth Ave., New York 3, 1952.

Frequently the law admits that it does not keep abreast of science and medicine explaining that it is neither immediately advised of progress nor convinced by competent authority of the authenticity and acceptance of new or recent medical and scientific concepts. "Psychiatry and the Law" represents an effort to acquaint the law with certain concepts concerning mental disorders in human beings. It attempts to place or have placed before the law information that it needs to accord certain medical principles the legal weight to which they may be entitled. The authors, one a lawyer and the other a physician, point out that the focus of the law is primarily on society and only secondarily on the individual; in psychiatry the emphasis is almost exclusively on the individual. To bring these views together and to increase cooperation between psychiatrists and lawyers, the authors say it is necessary to instruct lawyers in the fundamentals of psychiatry and to give physicians a real understanding of basic legal principles and methods. This book does just that. Almost one-half of it, written in language the judge, the lawyer, or the legislator can understand, is devoted to subjects such as personality formation, the psychoneuroses, the manic depressive and schizophrenic psychoses, psychopaths, sex offenders, organic brain disorders, and congenital intellectual deficiency.

The role of the psychiatrist in his formal association with the law is described. It is emphasized that the physician must know what information the law wants, if his knowledge and training are to be of value to the law. It is pointed out that there is a difference between criminal, civil, and administrative law and that each inquires into the mental capacity of a person according to his relation to society as he stands before the bar, be it as an accused, an aggrieved spouse, an heir, a prospective parent by adoption, or one facing commitment because of mental disorder. The authors discuss the position of the physician as a witness, under both direct and cross examination, and then they consider the use and abuse of hypothetical questions. The remainder of the book is a general discussion, for lawyer and physician, of veracity, mental competency, mental disorders, and the criminal and concludes with an excellent chapter entitled "An Ounce of Prevention." The book can be read and studied by both the physician and the lawyer. The lawyer, if he understands basic principles of psychiatry, and the physician, if he understands basic legal principles and practices, can express themselves with clarity. The two can, by intelligent and understandable questions and answers, convey to judge, jury, or legislative committee facts that will be meaningful and helpful in accepting and applying medical principles.

Modern Radiochemical Practice. By G. B. Cook, Ph.D., and J. F. Duncan, D.Phil. Cloth. $8.50. Pp. 407, with illustrations. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E.C.4, 1952.

This book, emphasizing the laboratory procedures of radiochemistry, is the necessary counterpart to the many books already available on the theoretical aspects of the subject. The introductory material is followed by chapters on the measurement of nuclear radiation, auxiliary electronic equipment, physical and chemical aspects of radioisotope production, errors in comparative and absolute counting, health precautions and laboratory design, and (a most valuable feature) directions for 30 experiments with radioactive substances. The book closes with a table of isotopes, an author index, and a subject index. It merits praise for the practical usefulness of its contents, for lucid writing, attractive printing, good diagrams, and extraordinary freedom from small errors.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

This Hospital Business of Ours. By Raymond P. Sloan. Cloth. $4.50. Pp. 331. G. P. Putnam's Sons, 210 Madison Ave., New York 16, 1952.

One might not expect a work of this type to be entertaining, but the lay reader will find it fascinating, and the trustee and hospital worker will find it very readable. The author is well qualified to write about hospitals and trustees and their duties and obligations. He is at present a hospital trustee, an editor of a hospital journal, and a writer and lecturer on hospital problems. The work has been wisely divided into two parts; the first interprets the hospital to the new trustee and to the layman as well. This orientation is basic and historical. In the second part, each chapter develops a phase of hospital mechanics and management concerning the trustee. All of these phases add up to "This Hospital Business of Ours." This second part is, in fact, a textbook for the sincere trustee.

As the author has stated before, hospitals are now in a transition period in which they are changing from charity institutions to business institutions, and this transition is taking place during an inflationary period. For such a period the work is timely, but, when this transition has become *fait accompli*, the book will still be a useful and important addition to hospital literature. It could be used as a textbook for students in hospital administration, and as a reference and guide in hospital administration, in lay education, and especially in the education of the trustee, since it would help him to function intelligently.

Something may have been read into the author's statements that he did not intend, but it seems that he asks or implies this question: "What are you, the hospital trustee, going to do about preserving our present free enterprise system of health service to the American people, to date the best system in the world?" This is a question worthy of careful study in times such as these. Every hospital trustee and administrator should read this book.

Fundamental Concepts in Clinical Psychology. By G. Wilson Shaffer, Professor of Psychology, Johns Hopkins University, Baltimore, and Richard S. Lazarus. Assistant Professor of Psychology, Johns Hopkins University. Cloth. $6. Pp. 540, with 15 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1952.

This is another book on "medical psychology" or "clinical psychology" designed as a textbook for the increasing swarms of undergraduate students of psychology who seem to be willing and anxious to undertake the psychotherapy of their impatiently waiting fellow men. The volume is an improvement on the average in its field, in that its initial chapters include a brief historical review of testing procedures and a relatively lucid critique of the methods of investigation employed, the nature of the evidence elicited, possible biases in evaluation of evidence, and the necessity for logical and configurational control of the inferences derived. Subsequent sections deal objectively and authoritatively with the realms in which psychologists have made their most valuable clinical contributions: the appraisal of intellectual skills, potentialities, and personality traits by the use of standardized scales or so-called projective techniques.

Thereafter, the content and style deteriorate rapidly into the usual overcondensed, academically stilted, and stereotyped descriptions of "psychotherapeutic devices," such as catharsis, suggestion, persuasion, and hypnosis. These descriptions are solemnly placed in artificially delimited categories that are neatly closed by separate critiques of each method. Dynamic approaches, including the theory and therapeutic applications of psychoanalysis and the modifications of Adler, Jung, Rank, Horn, and Alexander, are then discussed, with a predictable degree of thoroughness and penetration, in a total of 21 pages. Eight more pages are devoted to highly complex and contingent Meyerian procedures of distributive analysis and synthesis. As expected, Rogers' "client-centered therapy" (a name implying that in other therapies interest is somehow centered elsewhere than on the patient) receives commendatory emphasis, especially as applied to children. There is almost no recognition of the fact that this ostensibly "non-directive" approach consists in large

part of maneuvers that have been tried and either abandoned or greatly improved by others. Next a chapter attempts to deal with the techniques and results of all forms of shock therapy (including outmoded pentylenetetrazole [metrazol®]), psychosurgery, narcosis, artificial fever, drugs, and vitamins.

Finally, there is a section on the clinician in action that, unfortunately, does not do much to resolve the concern of the profession about the intent and implications of this and similar texts. Such concern will already have been aroused by statements such as "For the beginning student the book should serve as an introduction to later training and practice . . . and . . . should provide the foundation necessary for . . . the administration and interpretation of the technical instruments of diagnosis and the methods of conducting a therapeutic interview" (page *v*). "The role of the early psychotherapist was extremely directive as was the role of the general medicine man. . . . In contradiction to this point of view Rogers directed his attention toward assisting the individual to grow . . ." (page 387). "In the course of psychotherapy it may be necessary to refer the patient several times to medical specialists for the determination of organic complications. When such referrals are made, it is important that the consultant not become involved in the psychotherapy" (page 296). In effect, one of the fundamental concepts set forth in the book seems to be that this sort of training can prepare students without basic knowledge of physiology, neurology, differential clinical diagnosis, and medical therapy for careers as "psychotherapists," and that their judgment will then be sufficiently acute and reliable as to when and if to call on a physician as a consultant without permitting him "to become involved" in the treatment. The validity of such a thesis is highly debatable. As for the physical aspects of this book, the typography and index are excellent.

Tuberculosis. By Saul Solomon, M.D., Associate Visiting Physican, Fourth Medical Division, Bellevue Hospital, New York. Health Series, Harry Swartz, M.D., editor. Cloth. $3.50. Pp. 310. Coward-McCann, Inc., 210 Madison Ave., New York 16, 1952.

An informed nonmedical person with an interest in tuberculosis would find this volume worth his time. It is quite elementary for the physician, but it will give him the words to explain much about tuberculosis to his patients and friends. It is too technical and detailed for most patients to digest without help and might disturb those who misunderstand the variable factors in diagnosis, the basis of clinical classification, the fitting of therapy to both the patient and his tuberculosis, and the final rehabilitation of the individual in the community.

Some of the outstanding parts of the book are an excellent but brief history of the disease, a discussion of diagnosis and treatment in terms of anatomy, physiology, and psychology, a description of the drugs and surgical procedures in common use, and a bit on nonpulmonary tuberculosis. The book is concluded with a chapter on the eradication of tuberculosis as a public health problem, a glossary for the uninitiated, and an index for the student.

An Outline of General Physiology. By L. V. Heilbrunn, Professor of Zoology in University of Pennsylvania, Philadelphia. Third edition. Cloth. $10.50. Pp. 818, with 123 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

This book differs significantly from some other available textbooks of general physiology. The classic work on the subject by Bayliss was richly illustrated and owed its appeal, at least in part, to an abundance of historical and biographic material, some of it curiously irrelevant; other books have gone to the opposite extreme of philosophical and mathematical abstraction. Heilbrunn's book, though scantily illustrated, is distinguished by a stupendous wealth of quoted experimental facts, with references; it is well balanced and does not wander off into the vague or the whimsical. It is unusually well indexed and free from errors. It should prove invaluable to clinical investigators who, in connection with some problem of normal or abnormal physiology in man, wish to inform themselves about related problems in animals and plants.

Lehrbuch der Röntgendiagnostik. Von H. R. Schinz, W. E. Baensch, E. Friedl und E. Uehlinger. Nebst Beiträgen von E. Brandenberger, et al. 8. Lieferung: Innere Organe, mit Titelei, Inhaltsverzeichnis und Sachregister zu den Lieferungen 5 bis 8 und Autorenregister für das Gesamtwerk. Fifth edition. Paper. 96 marks. Pp. 3339-3792; lxxx, with 559 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

This eighth and final section completes a great textbook covering every phase of diagnostic radiology. This section deals with the colon, liver, bile ducts, gallbladder, spleen, pancreas, and urinary and genital tracts. The space devoted to the colon has been more than doubled since the third edition. Megacolon, hernia, various forms of colitis, diverticulosis, and diverticulitis are presented in conventional fashion, while sessile and pedunculated polyps and the malignant tumors of the colon are accorded the extensive discussion that their great clinical importance warrants. Following this are text and illustrations dealing with displacement and deformation of the colon by neighboring lesions and the appearance of colonic adhesions, radiation injuries, obstruction, foreign bodies, functional disturbances, diarrhea, and constipation. The pages on fistulas communicating with various parts of the alimentary tract, pneumoperitoneum, retropneumoperitoneum, and the liver are a serious attempt to say something about which there is, after all, little to say, but with their discussion of the biliary tract the authors return to important material that they handle with their usual validity and completeness.

Following a review of the anatomy and physiology of the gallbladder and bile ducts, there is an excellent discussion of the various types, sizes, and shapes of gallstones and of the conflicting theories about how and where they are formed. Cholecystitis, biliary fistulas, and the technique and findings in cholangiography close this portion of the work. Forty pages are devoted to the relatively sterile subject of the radiology of the spleen, pancreas, adrenals, and mesenteric lymph glands. One hundred and thirty pages of text and illustrations are devoted to the urinary tract and the male genital tract. On page 3603, figure 4528, three illustrations are printed upside down. Normal kidneys, congenital anomalies, solitary and multiple cysts, hydronephrosis, stone, infection, and neoplasm are well illustrated and described. The importance of the amputation of even a single calyx as evidence of tuberculosis is properly emphasized. X-ray pelvimetry, fetometry, and hysterosalpingography complete the radiological portion of the volume. The closing pages consist of a genetic consideration of diseases of the intestinal and urogenital tract.

Opiate Addiction: Psychological and Neurophysiological Aspects in Relation to Clinical Problems. By Abraham Wikler, M.D., Experimental Neuropsychiatrist, National Institute of Mental Health, Addiction Research Center, U. S. Public Health Service Hospital, Lexington, Kentucky. Publication number 161, American Lecture Series, monograph in American Lectures in Neurology. Edited by Charles D. Aring, M.D. Cloth. $3. Pp. 72. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1953.

This volume presents a concise account of our modern knowledge of opiate addiction. The vast literature on the subject has been reviewed and its cogent material set forth in an authoritative manner. The treatise is not intended to be an exhaustive presentation of the subject but, rather, is designed to interpret the past and present knowledge of addiction in terms of modern psychiatric and pharmacological concepts. The author treats the phenomena of emotional dependence, tolerance, and physical dependence on three levels of integration, namely, psychological, physiological, and biochemical. The pharmacological findings of the effects of opiates on laboratory animals are compared with corresponding findings in human beings. Of special interest is the newer work on N-allylnormorphine, which has been shown to immediately induce the withdrawal syndrome, and the mechanism of the action of morphine in the relief of pain. Barbiturate addiction and its comparison with opiate addiction are also included. Of special importance is the development of addiction patterns in relation to various occidental and oriental cultural habits. The style is lucid, and the book presents, in an authoritative manner, a well-documented and excellent survey of the problem of opiate addiction.

Atlas of Spatial Vector Electrocardiography. By J. Willis Hurst, B.S., M.D., and Grattan C. Woodson, Jr., B.S., M.D. Cloth. $6. Pp. 214. with 90 illustrations. Blakiston Company (division of Doubleday & Company, Inc.), 575 Madison Ave., New York 22, 1952.

This monograph is an extension of a recent presentation by Grant and Estes, in which they described their concepts and methods of approximate determination of spatial cardiac vectors in a simple and understandable way. Another presentation would be in order only if it made available either additional information or proof of the correctness of the concepts. This is certainly not the case in this atlas of spatial vector electrocardiography. The vectorial interpretation of the normal electrocardiogram and of six types of abnormalities are described and diagrammatically illustrated in the manner made familiar by the Emory school. The addition of tables of normal P-R and Q-T intervals taken from Ashman and Hull does not justify the misleading title of the book, which pretends complete coverage of the subject of electrocardiography.

The authors emphasize the didactic purpose of their presentation. In the preface they state that they feel justified "in sacrificing exactness in our efforts to explain the complicated electrical activity of the heart" and that "so many obvious simplifications are made that we are certain that such is not the case." It remains to be proved whether the method of teaching electrocardiography presented in this monograph is of greater value than the more orthodox empirical, analytic approach. The latter has as its purpose the presentation of the subject, to the student, with all its limitations and, to the practitioner, with all the variations actually found in practice.

The Principal Nervous Pathways: Neurological Charts and Schemas with Explanatory Notes. By Andrew Theodore Rasmussen, Ph.D., Professor of Neurology, Department of Anatomy, University of Minnesota, Medical School, Minneapolis. Fourth edition. Cloth. $4.50. Pp. 73, with 28 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1952.

Dr. Rasmussen has just recently retired as professor of neurology at the University of Minnesota. He has always been distinguished as a teacher of this difficult subject and has taken an active part in the training of many neurologists and neurological surgeons, particularly those who have received their training at the Mayo Clinic. This brief book of schematic drawings of the principal pathways of the nervous system has been an important adjunct to the author's teaching and to the teaching in many other institutions. One of the student's most difficult problems has always been acquiring a mental image of the long, intricate, and often tortuous pathways of the nervous system. Dr. Rasmussen presents them here in simplified and crystal clear form. He would be one of the first to insist that these few diagrams do not show the many minute, detailed, and complicated neural connections. This book is, as its title indicates, merely an elucidation of the principal pathways. As such it serves a very useful purpose. In this edition, Dr. Rasmussen has found it necessary to make very few changes. He has omitted the olivospinal tract because it is no longer believed to exist; the position of the cortical center for taste has been shifted; and a wider origin for the corticospinal tract has been indicated. It seems likely that the cortical origin for this latter pathway is probably even wider than this book would indicate.

Cardiographic Technique: A Manual for Cardiological Technicians. By S. L. Barron and A. Schott, M.D., M.R.C.S. Cloth. $5.50. Pp. 156, with 58 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

This little manual is intended primarily for use by electrocardiographic technicians. Mr. Barron worked for many years as a technician for the late Sir Thomas Lewis, and Dr. Schott is at present medical officer in charge of the cardiographic department of Queen Mary's Hospital for the East End (London). The use of unfamiliar British terms such as "valve-operated cardiographs" makes the text hard to follow. Emphasis is placed on the technical aspects of the string galvanometer recording photographically on bromide paper. The direct writing machines that are now commonly used and present many problems to the technician are dismissed briefly with the statement, ". . . very little servicing of these instruments should be undertaken by the technician." It is doubtful that technicians in this country will find much of value in this book.

A Method of Anatomy: Descriptive and Deductive. By J. C. Boileau Grant, M.C., M.B., Ch.B., Professor of Anatomy in University of Toronto, Toronto, Ontario. Fifth edition. Cloth. $7. Pp. 870, with 862 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1952.

Standard textbooks of anatomy, in general, are repositories of anatomic information that has accumulated through the ages. They tend to be encyclopedic, describing important facts and details with almost equal emphasis. They treat the complexities of the subject matter by systems rather than by regions, a procedure that is simpler for the author but that leaves the important task of correlating facts entirely to the student. Such traditional textbooks are useful, of course, for reference, but they fall short of being modern tools of learning because they generally fail to stress principles of anatomic relationships and to create functional understanding.

Professor Grant courageously abandoned such traditions. His "method" is an eminently readable textbook of human anatomy, written for the student rather than the practicing physician. Since its first appearance in 1937, the book has had 11 reprintings and 5 editions of which this last embodies considerable revision. It is deceptively simple in appearance but the "method" stands revealed on every page; it is the "method" of a great teacher with broad vision and excellent information from both the purely structural and the functional viewpoints. This book is truly a guide to anatomic reasoning and to understanding of the fabric of the human body. The subtitle "deductive anatomy" is appropriate, for the student will not find many burdensome anatomic minutiae but constant stimulation through emphasis of correlated facts.

The apparent simplicity of the book rests largely on the artistically unadorned but accurate illustrations. The line drawings are admirably suited for reproduction by the students in their learning efforts that, in anatomy more than in any other subject, should be one of visualization rather than of mere memory. The regional approach of the "method" is of advantage in the student's dissecting exercises. The first section of the book, however, gives a general account, with much valuable information, of the systems of the body. The terminology employed is the Birmingham revision of B.N.A. (Basle Nomina Anatomica). Fortunately there are few differences from the standard terms used in the U. S. There is an excellent index but, regrettably, no bibliography.

Neurosurgery in General Practice. By Adrien ver Brugghen, M.B., Ch.M., M.S., Clinical Professor of Neurological Surgery (Rush), University of Illinois College of Medicine, Chicago. Cloth. $14. Pp. 665, with 282 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1952.

The author presents a perspective of the problems that are encountered in patients who have traumatic or other lesions in the nervous system and who will ultimately be referred to a neurosurgeon. His purpose is to assist the general practitioner in the recognition of these problems and to explain to him the diagnostic and therapeutic methods of a neurosurgeon. In addition to the first eight chapters devoted to injuries to the brain, spinal cord, and peripheral nerves, there are chapters on trigeminal neuralgia, intractable pain, spinal cord diseases and tumors, cerebral, cerebellar, and pituitary tumors, cerebral vascular diseases, the sympathetic nervous system, congenital anomalies, spinal fluid, x-ray diagnosis, and neurological examination. Approximately one-fourth of the illustrations are x-ray photographs that clearly elucidate the text; the remainder are reproductions of gross and microscopic specimens, photographs of patients, and black and white line diagrams. There are few references, and those are selected for quick accessibility and general treatment of the subject matter under discussion. There is an adequate index.

There is little controversial material in the book, and, on the whole, the subject matter is adequately covered. The main criticism of the book is not in its content but in its stated purpose. The author states that there is nothing in the volume to interest a neurosurgeon and that it is primarily intended for the general practitioner. There is a great deal of value in the volume for a neurosurgeon. It is difficult, however, to see how the general practitioner will derive much benefit from it, unless he merely wishes to know how neurosurgeons work. For example, in the

discussion of acute head injuries, one of the problems that commonly confronts the general practitioner, there is nothing to indicate what he should do on his own or when he should refer the patient to the specialist. Similarly in considering rupture of the intervertebral disk, there is no discussion of conservative therapy. This is mentioned only in the misleading statement: "When a patient with these typical symptoms and signs does not respond to conservative medical management, a herniated nucleus pulposus should be very seriously suspected." The reader would infer from this statement that a ruptured disk never responds to conservative therapy. Other criticisms include a too-long discussion of pathological changes resulting from a brain tumor and an excessive number of illustrations of visual field defects. The chapters on neurological examination and diseases of the spinal cord are too brief to be of any value to either the general practitioner or neurosurgeon. The style of the writing is good, and the printing is excellent. The book can be recommended to neurosurgeons but it is doubtful whether it will be of any great interest or assistance to the general practitioner.

Outlines of Internal Medicine. Parts 1-5. Edited by C. J. Watson, M.D., Head, Department of Medicine, University of Minnesota, Minneapolis. Seventh edition. Cloth. $13. Pp. 178; 123; 119; 68; 113, with illustrations. Wm. C. Brown Company, Publishers, 915 Main St., Dubuque, Iowa, 1952.

This is a symposium in five parts, each written by a specialist in the given field. Dr. Watson is known as a medical educator, a member of the National Research Council, and a Fellow of the American Medical Association, the American College of Physicians, and of various other learned societies. He is well qualified to handle the great task set before him. The pages are large, and the text is divided into two columns, making easier work for the eyes. The type is sharp and distinct and is printed on paper of heavy, excellent quality. There is no index, but the table of contents is sufficiently detailed to help one to find the item desired. However, there are some deficiencies, particularly in the discussion of diseases of the nervous system. There is no reference to Parkinson's disease or to multiple sclerosis, which is said to be even more prevalent as a chronic condition than poliomyelitis. Poliomyelitis is discussed in one column, and, although this coverage is insufficient, one must remember that this book is an outline only, not a system of medicine. At the end of the description of each disease, there are copious references to source material. This book is not intended to be read as literature, but it is intended to be a vade mecum for consultation by the busy practitioner. Also, its size and weight make it better for reference purposes than for general reading. Part 5 is concerned with clinical chemistry and microscopy and covers urinalysis and examination of the blood, exudates and transudates, and spinal fluid. There are several blank pages for recording observations and laboratory notes. There is a list of the authors who have written articles especially for this volume.

Your Community's Health. By Dean Franklin Smiley, A.B., M.D., Commander, Medical Corps, U. S. Naval Reserve, and Adrian Gordon Gould, Ph.B., M.D. Revision of Community Hygiene. Cloth. $5.50. Pp. 454, with 121 illustrations. The Macmillan Company, 60 Fifth Ave., New York 11, 1952.

In this extensive revision of the book titled "Community Hygiene," which went through three editions, the authors have brought about many improvements. After a short introductory section dealing with history of the development of community hygiene, there is extensive consideration of methods now being employed to control health hazards in the environment. Included among these are recent problems that have come into sharper focus, such as air conditioning, soil conservation, housing, and accident prevention. In a third section, mental hygiene, sex hygiene, and care of the chronically ill are discussed. A fourth deals with methods of meeting needs of specific population groups, maternal and child groups, school children, rural and urban dwellers, and elderly persons. Agencies whose various services are available for solution of health problems are considered in the final section.

The book is well illustrated and is written in a readable style. At the end of each chapter, there are numerous suggestions for supplemental reading on the topic just considered. This is a good source of helpful information and guidance for the average person.

Lehrbuch der Anatomie des Menschen: Dargestellt unter Bevorzugung funktioneller Zusammenhänge. Band II: Eingeweide. Von Professor Dr. Alfred Benninghoff, Direktor an der Anatomie der Universität Marburg a.L. Fourth edition. Cloth. 39.60 marks. Pp. 568, with 330 illustrations. Urban & Schwarzenberg, Thierschstrasse 11, Munich 22; Meinekestr. 13, Berlin W. 15, 1952.

This is the second volume of a three volume work; Benninghoff considers this one the core of the set. He states that he has placed emphasis on functional anatomic relations. In this respect, this volume is specifically directed to those in the field of internal medicine. Chapters that are emphasized as important by the author include statics and dynamics of the abdominal cavity, the working rhythm of the liver, kinetics of the lungs, changes in the shape of the heart, and so-called defense mechanisms. The author has attempted to correlate function with anatomy. At the end of each chapter is a pithy and helpful summary that he has included by request of his students. It is gratifying to find brief yet terse discussions of embryologic origin and development immediately preceding the discussion of given organs. Some minor criticisms, which surely do not detract from this excellent work, are: a lack of true perspective in the presentation of the anatomic relations of the infundibulum of the gallbladder; a lack of proper presentation of the arterial supply, especially that involving the gastroduodenal segment; and a too abbreviated discussion of the vermiform appendix.

The volume is well printed on good paper, and the illustrations as well as the simple diagrams are also presented in admirable fashion. The book as a whole should prove to be a welcome addition to the library of one interested in anatomy, particularly that pertaining to the viscera. This textbook can be recommended for those who have a good reading knowledge of German.

Sexual Adjustment in Marriage. By Henry Olsen, M.D. Cloth. $6. Pp. 310. Henry Holt & Company, Inc., 383 Madison Ave., New York 17, 1952.

The author of this volume has been the physician in charge of sex hygiene instruction at the Continuation School of the municipality of Copenhagen since 1937. He has published numerous books on marriage, sex, and sex education. In the preface to this volume, the author states, "The Kinsey Report has created a general state of confusion with regard to a great number of sexual questions in America" and then, in a similarly unrealistic fashion, he compares these problems in the U. S. to those in Denmark 20 years ago: "The American situation of today closely approaches that which we experienced in Denmark about 20 years ago. The field of sexual education is, in fact, one field in which the United States lags."

This book is divided into 67 short chapters, many of which are devoted to anatomy, physiology, and pathological changes of the sex organs of men and women. Others, include information regarding physical hygiene, the sexual education of children, and pregnancy and childbirth. The emotional aspects of sexual life are presented in terms of an out-moded, rationalistic psychology not in keeping with present scientific knowledge. Although written for popular consumption, many of the chapters would be of interest to students of medicine, not to the average layman. This book cannot be recommended to those who wish to obtain correct information regarding sexual adjustment in marriage.

Human Milk: Yield, Proximate Principles and Inorganic Constituents. By S. D. Morrison, B.Sc. Technical communication no. 18 of Commonwealth Bureau of Animal Nutrition, Rowett Research Institute, Bucksburn, Aberdeenshire, Scotland. Cloth. $1.50; 10s. 6d. Pp. 91, with 12 illustrations. Commonwealth Agricultural Bureaux, Farnham Royal, Slough, Bucks, England, 1952.

Although this is a very small book it contains a great amount of information on an old subject, human milk. It contains much original research and six pages of bibliography. Two main chapters cover the volume of milk, with remarks and studies on the various factors that might affect that volume. The remainder of the book is devoted to an exhaustive study of the composition of milk. This publication is highly technical and contains many graphs and tables, which should be of great use to those who are interested in infant feeding and to those who are teachers in pediatrics.

Electrocardiography in Practice. By Ashton Graybiel, M.D., Captain, Medical Corps, United States Navy, Paul D. White, M.D., Executive Director, National Advisory Heart Council, Boston, Louise Wheeler, A.M., Executive Secretary, Cardiac Laboratory, Massachusetts General Hospital, Boston, and Conger Williams, M.D., Instructor in Medicine, Harvard Medical School, Boston. Third edition. Cloth. $10. Pp. 378, with 294 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, 1952.

This book has been rewritten to include information on the early development of electrophysiology and facts regarding the classical and unipolar leads. Recent practical advances in clinical electrocardiography are presented. Electrical orientation of the heart is discussed, but vectorcardiography is not yet considered practical for clinical use.

The book is divided into eight parts: introduction; method; normal electrocardiogram with variations; disorders of rhythm and conduction; changes caused by drugs and chemicals; electrocardiographic patterns; etiological types including congenital, hypertensive, coronary, and rheumatic heart disease, subacute bacterial endocarditis, cardiovascular syphilis, diphtheria, other infections, endocrine disorders, and cor pulmonale; and a final portion including "unknown" electrocardiograms for practice interpretation. Standard terminology is used except for the substitution of atrium for auricle. The format is good, but the size could be reduced for convenience. The index is good, and the few diagrams are clear. All other illustrations are of string recorded graphs on a good quality of paper with adequate legends providing clear analysis and interpretation correlated with history and findings. The book is not intended to be a textbook, but will serve admirably as an atlas.

Introduction to the Interpretation of the Electrocardiogram. By Louis N. Katz, A.M., M.D., Director, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago, Richard Langendorf, M.D., Research Associate, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, and Alfred Pick, M.D., Assistant Cardiographer and Research Associate, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital. University of Chicago Committee on Publications in Biology and Medicine. Paper. $2.50. Pp. 78, with 61 plates illustrating more important deviations from normal, selected from files of Michael Reese Hospital. University of Chicago Press, 58th St. and Ellis Ave., Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W.1, 1952.

This booklet was designed by the authors for the physician who does not specialize in cardiology and for the student who is beginning his studies in cardiac physiology. The principles of electrocardiography are discussed briefly. There is an excellent chapter on the step-by-step procedures to be followed in reading an electrocardiogram. Then there is a table listing the characteristics of the normal electrocardiographic cycle. The rest of the booklet consists of 60 plates illustrating important electrocardiographic abnormalities. The descriptive material accompanying each plate is concise and easily understandable. The authors, all well-informed and competent cardiologists, have done a splendid job in simplifying a complicated subject for those who would like to have authoritative information on electrocardiography but do not wish to go into the subject too deeply.

Die Leistungen des Nervensystems: Auf Grund anatomischer, experimenteller und klinischer Tatsachen dargestellt. Von Dr. med. Johann Gottschick, Oberarzt und Medizinalrat an einem Niedersächsischen Landeskrankenhaus. Cloth. 42 marks. Pp. 766, with 244 illustrations. Gustav Fischer, Villengang 2, Jena 15b, Germany, 1952.

This is a voluminous monograph on the functional activity of the nervous system. It is conservative and orthodox in its viewpoint and in the material it presents. Its 20 chapters deal with the various subdivisions of the nervous system beginning with the neuron and then the peripheral nervous system, including the autonomic system. The spinal cord, the organs of the special senses, the brain stem and cerebellum, and the cerebral cortex are considered. The monograph ends with a chapter on the conditioned reflex. The section on the spinal cord follows strictly Sherringtonian lines, while that on the cerebral cortex accurately presents the views of Brodmann, the Vogts, von Economo, and Koskinas. The more recent work of Bailey and von Bonin on the cytoarchitecture of the cerebral cortex, which does not support the extensive subdivisions of the earlier workers, is not mentioned. It is rather remarkable, in the chapters on the rhinencephalon and the temporal lobes, that the author does not mention the penetrating theoretical considerations of Prof. J. W. Papez (A Proposed Mechanism of Emotion, *Arch. Neurol. & Psychiat.* **38**:725-743 [Oct.] 1937), which preceded the actual experimental demonstrations that this part of the brain is concerned with emotional expression. The author does not point out the apparently contradictory facts that extirpation of the temporal lobes in the cat results in a vicious animal whereas a similar extirpation in the monkey produces a docile animal.

There is an extensive bibliography and a satisfactory index. This is a scholarly review and condensation of much of the literature of the world on the physiology of the nervous system. It is in no way a presentation of original material. Although the author has reviewed the literature from many countries, he has drawn heavily on the work of investigators in the United States. This book is very similar in content and organization to Fulton's *Physiology of the Nervous System*, which has passed through several editions since it first appeared in 1938.

Oestrogens and Neoplasia. By Harold Burrows and Eric S. Horning. With contributions by W. C. J. Ross and C. W. Shoppee. Cloth. $6.75. Pp. 189. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1952.

This monograph is an authoritative review of the scientific literature on the effects of estrogens on tumor formation of the various organs and tissues of the body. It includes descriptions of the chemical nature of the estrogens, their sources, and their influences on normal tissue response. The effects of the estrogens on tumors of the pituitary, ovary, testis, adrenal glands, and urogenital organs, such as the prostate, uterus, and breasts, are thoroughly discussed. Considerations of the hereditary factors in breast cancer are also detailed. Treatment of cancer is discussed in the light of the knowledge acquired on the influence of estrogens on these structures. This excellent monograph discloses an enormous amount of information present in the literature and includes considerable data contributed by the authors themselves.

This volume should be an excellent source of reference material for physicians who are especially interested in this field as well as to researchers in the laboratory and the clinic. Because of the complexity of the studies and information described, the monograph cannot be considered suitable for the average physician or practical as a guide to therapy. It serves a most useful purpose, however, by presenting clearly and with good judgment almost all of our knowledge on the indicated subjects in one volume.

Forensic Psychiatry. By Henry A. Davidson, M.D. Cloth. $8. Pp. 398. Ronald Press Co., 15 E. 26th St., New York 10, 1952.

"Forensic Psychiatry" is written by a physician primarily for any other physician who may be called on to tell courts and administrative tribunals of his medical diagnoses and treatments. It is designed to assist the physician examine a patient or claimant, evaluate disability, measure responsibility, or prepare a report for a legal rather than a medical reason. An attempt is made to establish a bridge of understandable communication between medicine and the law. Forensic psychiatry is explained in its several phases: criminal responsibility, personal injury evaluation, placement and custody of children, last wills and testaments, sex offenses, alcoholism, juvenile courts, commitment procedure, and competency in civil law. The nature of medical testimony, preparation for court appearances, hospital and office records, and the translation of technical terms are discussed in such a manner that the physician is enabled to prepare and present complete and convincing testimony. In the chapter entitled "The Psychiatrist and the Juvenile Court," the manner in which a physician is acquainted with his duty to aid the law is exemplified by the recitation of section headings, such as anatomy of the juvenile court, place of examination, examination of juvenile offenders, and murders by juveniles. Glossaries of legal and psychiatric terms reduced to everyday language complete the book.

QUERIES AND MINOR NOTES

OCCULT SPINA BIFIDA

TO THE EDITOR:—*A 6-year-old boy was born with an occult spina bifida and bilateral clubbed feet. He has had corrective operations and several castings for the feet, without much benefit, and he has had an exploration of the spinal cord. The child walks with metal braces applied to the shoes, by swinging widely from the hips. The main problem is complete incontinence of urine and feces. An attempt was made to fit him with a penis clamp, but the penis was too small to hold the clamp. Can anything be done for this child? Would there be any rationale for endocrine therapy in an attempt to promote growth of the penis so a clamp might be used? Is there any possibility of muscle transplantation for urinary and bowel control? Would it be advisable to do a colostomy?*

M.D., Washington.

This inquiry was referred to three consultants, whose respective replies follow.—ED.

ANSWER.—Occult spina bifida and an apparently inadequate nerve supply to both bladder and large intestine in a 6-year-old boy presents one of the most difficult neurological and urological problems. The fact that the patient had corrective treatment of the orthopedic condition with an exploration of the spinal cord suggests that any surgery to relieve pressure on the nerve roots of the lower spine is out of the question. In the past, some of these patients were benefited by so-called presacral neurectomy. From the description given in this case it would seem that this type of surgery would not help. The problem of complete incontinence of urine and feces is most difficult. In this case, it would be important to determine whether the incontinence of urine was due to a paralytic bladder with a paradoxical overflow of urine or whether it was due to a complete destruction of the sphincter. If this is due to a paradoxical incontinence and the patient is carrying a large amount of residual urine, the only rational treatment for the time being would be a permanent suprapubic cystotomy. Transplantation of the ureters to the bowel in this case would undoubtedly lead to rapid development of bilateral pyelonephritis. There probably is a lack of proper innervation of the ureters as well as of the bladder. Doing a colostomy in this case is completely out of the question. The incontinence of feces is not a lethal condition, whereas the urinary incontinence may prove to be lethal if, after a time, residual urine in the bladder causes sufficient back pressure on both kidneys to cause bilateral renal insufficiency.

ANSWER.—In view of the fact that the spinal canal has already been explored and it has not been possible to do anything to improve this child's condition, there is nothing further than can be done from a neurological or neurosurgical standpoint.

ANSWER.—It is to be presumed from the description given that this boy's condition may be deteriorating. Ultimately, malfunction of the urinary system will lead to ascending infection and uremia. It should be definitely decided whether he has a malformation of the spinal cord, such as hydromyelia, in association with the spina bifida occulta or whether the process of growth is causing increased traction on adhesions associated with the bony deformity, thereby compromising the circulation of the spinal cord and causing the neurological signs reported. A spinal cord tumor must be ruled out. A teratoid tumor or teratoma may have escaped notice at the time of the spinal exploration. Diastematomyelia, existing at a higher level than that at which the exploration was done, could cause this picture. It is advised, therefore, that this child be reviewed by a neurosurgeon, a genitourinary surgeon, and a pediatrician, and that the orthopedic surgeon continue in support. The neurological examination cannot be considered complete until a detailed roentgenographic study of the entire spine has ruled out diastematomyelia. Supplementary myelographic, intravenous pyelographic, cystometric, cystographic, and urethrographic examinations may be essential before a conclusion can be reached. The pediatrician or family physician, led by the patient's general physical status, blood chemistry and cytology, must at all times pass on whether these special examinations will place the patient in jeopardy. It has been the experience of this consultant that some patients in as much difficulty as this boy have been restored to a normal status when the cause of the neurological deficit was identified and treated. Until further consultation has been obtained and studies as outlined completed, plans for mechanical or operative means of gaining excretory continence should be deferred. All transplants, especially ureterointestinal, have proved to be of doubtful efficacy in the face of increasing neurological deficit when the rectal sphincter is incompetent. Major orthopedic procedures can be deferred for several months, temporizing physical therapy procedures being used meanwhile. Any endocrine therapy should be deferred until neoplasm is ruled out.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

PELVIC PAIN AND INFERTILITY

TO THE EDITOR:—*A woman, aged 28, had a laparotomy after the birth of her second child in 1949, because of "soreness" in the region of the right adnexa. The right ovary was found to be replaced by a large cyst, and there was bilateral hydrosalpinx without evidence of tubal infection. The right ovary, both tubes, the appendix, and about one-third of the left ovary were removed. Since the operation, the patient has had increasing difficulty about two days prior to menstruation and for the first two days of menstruation. The tenderness persists in the same area, and there is moderate dysmenorrhea. A bolus of feces passing that area gives the same tender sensation. I have tried every treatment that has been advocated, and the best results have been obtained with cortisone. I believe that a laporotomy should be done. The patient is interested in becoming impregnated by manual implantation of the ovum, obtained by culdoscopy, in the uterus. I have tried to discourage use of such a procedure, but I need help.*

M.D., Mississippi.

ANSWER.—The exact location of the tender area is not stated in the query. Regardless of where it is, the patient's desire for a baby is apparently greater than the wish for surgical relief of the pain. In the present state of our knowledge, manual implantation of an ovum from the ovary into the uterine cavity in humans is not feasible. It has apparently never been carried out. Since both tubes have been removed and the uterine cornua are sealed off, as can be determined by a Rubin test or a hysterosalpingogram, there are only two operations that can be done in an attempt to overcome the patient's infertility. One is to resect a cornu of the uterus and implant the remaining ovary or a part of it over the cornual opening (Estes operation), and the other is to implant the ovary in the uterine cavity (Tuffier operation). The results with both of these operations are so poor that there is hardly any justification for their use. The patient should try to adopt a baby. If the pain becomes severe enough to influence the patient in favor of a laparotomy, a careful exploration must be carried out to try to find the cause of the pain. If the pain continues in the midline of the pelvis regardless of what is done, a pelvic sympathectomy should be done also, because this operation often relieves obscure pains in the pelvis and dysmenorrhea as well. Since the patient is only 28 years old, the remaining ovary should not be removed. If the operator is convinced that the ovary is the source of the patient's pain, an ovarian sympathectomy should be carried out, that is, the ovarian blood vessels on the side of the remaining ovary should be ligated and cut.

SWIMMING POOL REGULATIONS

TO THE EDITOR:—*Should high school pupils be required to use soap when they take a shower before entering the swimming pool? Should girls who are menstruating be allowed to go into the pool, and, if so, should they be required to use tampons?*

L. C. N. Wayland, M.D., Santa Barbara, Calif.

ANSWER.—Soap and water go together. This is particularly true if cleanliness, personal hygiene, and sanitation are part of the physical education program in which this high school swimming pool is used. The school should buy soap that will lather well in the water provided for the showers and require a bath with soap, as well as the removal of all soap before entering the pool. Water, without soap, would hardly be adequate for removal of the dirt accumulated by the typical youngster.

No general rules can be made for physical activity (including swimming) during menstruation. Some girls can be active with comfort, others cannot. The Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association states in its 1951 report, "The Physical Educator Asks About Health," "Medical opinion advises that, except for strenuous activities that involve considerable competition during the first two days of this period, exercise is generally beneficial because it stimulates circulation and prevents congestion which is one of the causes of discomfort. Each girl's own experience should guide in determining the amount of activity that is desirable for her." A menstruating girl entering a swimming pool does not create a hazard to the health of others but produces a situation that is aesthetically undesirable.

A school may require the use of tampons for pool entrance by menstruating girls, but it should provide for excuses from swimming for those who find tampons undesirable or unsatisfactory. The Joint Committee on Health Problems in Education, basing a statement on the published observations of Dr. Robert Latou Dickinson, notes that, although tampons are generally acceptable and satisfactory to 9 out of 10 girls, there are some who need more protection for the first one or two days, some who find tampons uncomfortable, and a few who feel they produce cramps.

TETANUS PROPHYLAXIS

TO THE EDITOR:—*Some surgeons think that tetanus antitoxin should no longer be used, since one penicillin injection administered shortly after an injury fully prevents tetanus. Is this an authoritative opinion? If it is correct, how soon after an injury must the penicillin be given? Tetanus antitoxin is generally considered effective when given as late as 48 to 72 hours after the wound has been sustained.*

Walter Newman, M.D., Springfield, Mass.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—Penicillin is not a reliable substitute for tetanus antitoxin. It would be dangerous to assume that tetanus antitoxin is not required for passive immunization. It has been stated that the incubation period for tetanus may be as short as one day; the average time is from one to two weeks.

ANSWER.—This consultant has seen fatal clinical tetanus develop in a child given multiple large doses of penicillin promptly after sustaining a compound fracture of the arm. A recall injection of tetanus toxoid instead of tetanus antitoxin was given at the same time because of misinformation about previous immunization. Moreover, evaluation of a report by Taylor and Novak (*Ann. Surg.* 133:44, 1951) indicates that the sole use of penicillin in prophylaxis against tetanus is not approved, but that penicillin may be used locally and systemically in conjunction with tetanus antitoxin or toxoid or both, as indicated. Medicolegally it would be difficult to justify the exclusion of the more specific agents, tetanus antitoxin or toxoid, already tested both experimentally and clinically, in favor of penicillin prophylaxis, a technique still in the stage of laboratory investigation.

No definite limit can be placed on the period during which tetanus antitoxin is able to prevent or modify the course of clinical tetanus; however, when prophylaxis is delayed the prophylactic dose should be increased. Under all circumstances, doses of 5,000 to 10,000 units (American) are to be employed; amounts up to 20,000 to 40,000 units are justified if there is delay. Moreover, even in those who have had previous injections of tetanus toxoid, the simultaneous use of antitoxin and recall injections of tetanus toxoid is indicated when the following conditions are present: delay in prophylaxis, multiple wounds, debility from various causes, or great loss of blood. Recall injections of toxoid are satisfactory under ordinary circumstances, despite the passage of as many as 10 years following basal immunization. The exact duration of immunity after recall injections is subject to such individual variation as to justify small booster doses for each indication.

A large body of data testifies to the value of specific prophylaxis. To eliminate the occasional failures, improvement in present techniques must be formulated, i. e., increases in the dosage of tetanus antitoxin, reformulation of the indications for prophylaxis, and modifications in the programs of active immunization. To repudiate tetanus antitoxin and toxoid in favor of penicillin would seem to be a grave mistake, at least at our present state of knowledge.

EPILEPTIC DRIVERS OF AUTOMOBILES

TO THE EDITOR:—*A patient who has epilepsy of unknown origin refuses to quit driving his car. It seems that I have a moral obligation to notify the commissioner of motor vehicles so that his license may be revoked for his own protection and that of others on the highway. On the other hand, the diagnosis of this man's condition is confidential information and may not be divulged without his consent, which he will refuse. What is the proper course of action in this case?*

M.D., New York.

ANSWER.—This question might be put to the council on ethics; however, certain background information is pertinent to the problem. In five states the matter of confidential information is not pertinent, because the physician must report cases of epilepsy as he reports smallpox and syphilis, even for infants and the aged. Benefit to the public is questionable, because affected persons will avoid seeking the medical advice they need, thus increasing the hazards of driving. New York State is more stringent than most in requiring a two year period of freedom without medication. This proviso is equivalent to one that would require that a person with defective vision not wear glasses. Risk to the driver and the public depends on a number of factors, of which the period of freedom is only one. Danger is modified if attacks occur only during sleep, if there is an adequate warning, if the electroencephalogram is relatively normal, and if the person is following up-to-date medical advice and is avoiding conditions that might increase liability to accidents. Even the necessity or usefulness of the driving might be given consideration. If the physician feels that his moral obligation impels him to report a patient subject to epileptic seizures, he should also report other patients whose control of consciousness and muscles may at times be impaired: certain diabetics and persons with heart disease, the mentally disturbed, and, most dangerous of all, the alcoholic. Certainly the physician should insist that the uncontrolled epileptic and these others should not drive, and he may refuse further services if they do. From that point his conscience and good sense (aided by any official pronouncement that may be made) must be his guide.

LOBAR PNEUMONIA

TO THE EDITOR:—*Do the lungs in cases of true lobar pneumonia of pneumococcic etiology go through stages of engorgement, red hepatization, gray hepatization, and resolution, or is the pathological process arrested at whatever stage it happens to be in at the time adequate therapy and resolution begin?*

M.D., Illinois.

ANSWER.—It is believed that, when adequate doses of penicillin are given to a patient suffering from pneumococcic lobar pneumonia, resolution begins as soon as the pneumococcic process is under control. The normal progression of the pathological process through its classical stages is arrested. The earlier the antibiotic is administered the faster the infectious process is arrested and the sooner the lung tissue will return to a normal state.

THE ERYTHROCYTE SEDIMENTATION TEST

TO THE EDITOR:—*In almost every case report in medical journals my attention is called to the erythrocyte sedimentation rate. I have been slow in accepting it as having any special significance. Please discuss this subject at some length.*

Ben D. Baird, M.D., Galesburg, Ill.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—The erythrocyte sedimentation test measures the rate of fall of red cells suspended in whole blood to which an anticoagulant has been added. As used in clinical medicine, the sedimentation rate usually serves as a semiquantitative test for the concentration of fibrinogen in the plasma, since the level of this globulin is frequently elevated. This is a nonspecific change comparable to leukocytosis and to fever. An increase in plasma fibrinogen occurs as a regular change in most infections, following injury to tissue, following necrosis such as that caused by coronary thrombosis, in many instances of cancer, following operative procedures, and accompanying normal pregnancy during the third trimester. An increase in the level of serum globulins also is associated with an increased sedimentation rate and may be observed in such conditions as cirrhosis of the liver and other diseases causing hyperglobulinemia. The test does not, therefore, make any single diagnosis but is a screening procedure that may aid in the detection of some abnormality requiring further study.

ANSWER.—Since a wide difference of opinion exists regarding the diagnostic and prognostic value of the erythrocyte sedimentation rate, it may be well to review some of the factors that affect this phenomenon.

Technical factors include the following ones: (1) the anticoagulant used: sodium citrate (Cutler method) slows the rate, whereas the balanced mixture of ammonium and potassium oxalate (Wintrobe method) does not affect the rate; (2) the bore and length of the tube: short tubes introduce the factor of progressive concentration of cells with consequent slowing; tubes less than 2 mm. in diameter will slow the rate of sedimentation because of the influence of capillary action; (3) position of the tube: inclination of the tube from the vertical position greatly increases the rate of fall of the erythrocytes; it has been estimated that a deviation of only 7.5 degrees may produce an error up to 100%; (4) temperature at which the test is conducted: temperatures between 30 and 42 C tend to decrease the rate; room temperature of 20 to 25 C is said to be satisfactory; (5) venous stasis in obtaining the test sample may greatly affect the sedimentation rate by increasing the erythrocyte and protein content of the blood; (6) allowing the sample to stand at room temperature longer than three hours before setting up the test will reduce the sedimentation rate.

Physiological or pathophysiological factors altering the erythrocyte sedimentation rate include the following factors: (1) sex: there is no difference between normal boys and girls before puberty, but the rate is higher in adult women than in adult men; this appears to be related to hemoconcentration; (2) pregnancy distinctly causes an increase in the sedimentation rate; (3) changes in the plasma proteins affect the sedimentation rate; an increased fibrinogen and/or globulin level will elevate the rate, while an increased albumin level slows the rate; (4) there is some evidence that an increased cholesterol level increases the sedimentation rate, while an increased lecithin level is said to decrease the rate; (5) hemoconcentration slows the rate, while hemodilution or anemia increases it; cell shape, however, is also a factor, so that sickled cells have a decreased rate of fall, presumably due to interference with rouleau formation; correction charts constructed to compensate for the effect produced by anemia have not been entirely satisfactory.

It should be obvious from the foregoing that the erythrocyte sedimentation rate is completely nonspecific. Nevertheless, claims are still made for its diagnostic value; for example, it has been stated that the test will differentiate between organic and functional disease and between ectopic pregnancy and chronic pelvic inflammatory disease. Many examples of organic disease in which the sedimentation rate is normal could be given as well as instances of functional disease in which it is normal or elevated. A patient's diagnosis is no longer relegated to the functional category simply because of a normal sedimentation rate and the physician's inability to detect organic disease. A diagnosis of functional disorder is, of course, a positive diagnosis. Thalhammer and Janicek (*Wien. klin. Wchnschr.* **63**:116, 1951) recently observed that pneumoencephalography is often followed by an elevation of the sedimentation rate. This observation was independently confirmed in some but not all of a group of patients undergoing this procedure (Zarafonetis, C. J. D.; Murtaugh, F., and Reuter, R.: unpublished data). Although the mechanism for this change is obscure, the implication that the central nervous system can mediate a change in the sedimentation rate casts further doubt on the validity of its use in the differentiation between organic and functional states. With regard to ectopic pregnancy and chronic pelvic inflammatory disease, the test can be of little value, since the latter condition is one of the important predisposing factors for the development of ectopic pregnancy.

There are many physicians who, recognizing the nonspecificity of the test, do not use the erythrocyte sedimentation rate for diagnosis but claim it to be of real value in estimating the prognosis of a patient's illness. This belief is predicated on the fact that an elevated rate is present in most patients with diseases such as acute myocardial infarction, acute rheumatic fever, active rheumatoid arthritis, active tuberculosis, and many others. The sedimentation rate generally declines to a "normal" level on recovery from the acute process. Unfortunately, many exceptions have been observed in connection with the prognostic accuracy of the sedimentation rate. A few specific examples may be cited: Carletti and Fusari (abstracted, *J. A. M. A.* **150**:1351 [Nov. 29] 1952) studied 81 children with tuberculous meningitis and stated, "Since there was never a relationship between the erythrocyte sedimentation rate and the course of the disease, the condition of the spinal fluid, and the other localizations involved, the test has no prognostic value during streptomycin therapy of tuberculous meningitis with or without pulmonary involvement." Wells and associates (*Am. J. Clin. Path.* **21**:423, 1951), in following the course of treatment in rheumatoid arthritis, state, ". . . we rarely find it necessary to rely upon any other evidence than that furnished by the clinical appearance of the patient, the blood count and the urinalysis. We do sedimentation rates but we are no longer surprised when they fail to correlate with obvious changes in the patient's clinical condition."

In actual practice, therefore, repeated determinations of the sedimentation rate in a given patient may at times give results that are not compatible with the clinical progress. Thus, the clinician either subordinates his clinical opinion or rejects the sedimentation rate determination as an "artifact" or a "laboratory error." In some instances, unexpected results have been attributed to differences in method, e. g., the Wintrobe versus the Cutler method. While the chance for technical error is great and different methods naturally give different rates of sedimentation, the test has shown bizarre results even under carefully controlled conditions. In a hematological laboratory daily determinations employing a standardized technique have been made in many research subjects. Occasionally, patients with repeatedly high sedimentation rates have at times, for no apparent clinical or laboratory reason, shown no settling of the red cells whatsoever. The following day, the sedimentation rate usually was again rapid. Additional tests in hundreds of apparently normal students have often yielded abnormal sedimentation rates. After clinical study, usually no nosological explanation was found, and the individual student's activity was not restricted. As currently employed, the erythrocyte sedimentation test is accepted or rejected by clinicians because its results do or do not fit their respective clinical impressions. Interpretation of the test is, therefore, largely subjective.

Further insight into the erythrocyte sedimentation phenomenon may be had by recalling a part of its history, which extends back 2,500 years. According to Muller (Clinical Significance of Blood in Tuberculosis, New York, Commonwealth Fund, 1943), in ancient times drawn blood was allowed to clot and was found to separate into four layers (the humors). "Disease was supposed to arise from a faulty admixture of the four fluids of the blood, the commonest fault being an increase of

phlegm. As the buffy coat or phlegm was most strongly developed in diseases with a quantity of excretion of pus from body surfaces or lungs, the idea became prevalent that these excretions consisted of the phlegm in the blood. This theory of disease developed by the Greeks reigned supreme for many centuries, and blood letting became the order of the day both for diagnosis and as a therapeutic measure to remove noxious material." The use of the erythrocyte sedimentation rate appears to have evolved from this ancient medical philosophy. It cannot be substituted for a complete history and physical examination, specific laboratory studies, and careful follow-up of the patient. The conclusion that it is inconceivable that a phenomenon influenced by many variable factors should be of appreciable diagnostic and prognostic value is justified, in this consultant's opinion.

PROPHYLAXIS OF RESPIRATORY TRACT INFECTIONS

To the Editor:—*Is it safe to give oxytetracycline ("terramycin") in doses of 250 mg. twice a day to a child weighing 37 lb. (16.8 kg.) for prevention of respiratory tract infections, to which the child is highly susceptible?*

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Answer.—Administration of 500 mg. of oxytetracycline per day for the prophylaxis of respiratory tract infections represents a total daily dose of about 13.5 mg. per pound, or about 30 mg. per kilogram of body weight. This dosage is generally recommended for the treatment of moderately severe infections and would appear to be definitely high. There is question about whether antibiotics should be used at all in the prophylaxis of respiratory tract infections. The majority of such infections are produced by the viruses of the common cold and influenza and by viruses as yet uncharacterized. Clinical or experimental evidence does not exist that shows the efficacy of antibiotics in the prophylaxis or therapy of viral infections of the respiratory tract other than those produced by the virus of primary atypical pneumonia. The repeated use of antibiotics in any person increases the chance that that person will become sensitized to one or more of the antibiotics employed. While there is some reason to consider the use of antibiotics in the prophylaxis of secondary bacterial infection in respiratory tract infections in certain debilitated patients or in those who are a special risk or in the prophylaxis of beta hemolytic streptococcic, pneumococcic, and Vincent's infections in exposed persons in localized epidemics of these infections, the general use of sulfonamides or antibiotics in the prophylaxis of respiratory tract infection cannot be recommended.

SERVICING A FLUORIDATING MACHINE

To the Editor:—*Is it possible for a workman at a machine that adds fluoride to a city's water supply to inhale enough of the chemical to contract toxic hepatitis? A workman has noted browning of all his teeth since he has worked near this machine during the past six months.* *M.D., Idaho.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is no reason to suspect that toxic symptoms will develop in a workman servicing a fluoridating machine in a water plant, if ordinary precautions are followed. Under recommended procedures of the American Water Works Association (*J. Am. Water Works A.* **41**:575-579 [July] 1949) it is stated, with respect to application of fluoride, "7.2. Special precautions must be taken to protect the operators from inhaling fluoride dust when charging the hoppers of the feeders. It is recommended that dry feeders be equipped with dust collectors consisting of bag filters operating under positive air pressure and vented to the outside. Each operator who handles fluoride should be provided with his individual toxic-dust respirator to be used only when handling the chemical." The browning of all of the teeth is not due to possible inhalation of fluoride dust. Endemic dental fluorosis is a developmental defect, a hypocalcification or hypocalcification and hypoplasia, that occurs during the period of tooth calcification. In areas with water of high fluoride content, persons with moderate or severe hypocalcification may get posteruptively a brown stain. The hypocalcified condition of the enamel is, however, a prerequisite for the development of the brown stain. Dental fluorosis or mottled enamel never develops in a person moving into an endemic area after the teeth have formed and erupted.

Answer.—This inquiry has nothing to do with the physiological action of fluoride on the consumers of water in the area mentioned. The question, "What will the effect be on the man who adds fluorides at the water works to prevent caries in the children of a community?" was bound to arise. The situation already has been faced. Zufelt (*Water and Sewage Works* **97**: 335, 1950) has made various determinations at a water works plant. He found in the general atmosphere 0.025 to 0.134 mg. of fluoride per cubic meter of air for routine operations. The commonly accepted allowable concentration is 2.5 mg. per cubic meter; however, at the immediate time of dumping barrels of fluoride into a hopper, the atmospheric concentration reached 8.89 mg. per cubic meter. The urine of water works plant workers varied from 0.1 to 1.58 mg. of fluoride per liter of urine. The upper limit of safety is about 2 mg. per liter. In the instance described, no information is furnished about frequency and length of exposure and concentration of the dust. Damage to the liver is possible but is far less common than nephritis. Many fluoride-exposed workmen complain of pain in the liver region in the absence of a demonstrable pathological condition. If the conditions of work are still suspected, many examinations might contribute information; these would include roentgenologic examination of bones (ribs, spine, and pelvis) for indications of osteosclerosis, determination of urine fluoride level, determination of atmospheric fluoride, and dental examination to determine whether the fluoride mottling was actually a recent occurrence.

ELECTROCARDIOGRAMS FOR SCREENING PURPOSES

To the Editor:—*In what age groups would you consider it advisable to make routine electrocardiograms of the general population for screening purposes? What is the least number of leads that may be employed, and which are preferable? Of the 12 leads ordinarily obtained, which would most likely provide the greatest number of abnormal tracings?*

M.D., New York.

This inquiry was referred to three consultants, whose respective replies follow.—Ed.

Answer. — Electrocardiographic anomaly without clinical signs and symptoms is most likely to be found in persons between 40 and 60 years of age. The most informative leads are usually the three standard leads (1 to 3), lead aVF, and leads V1, V2, V4, and V6. The minimum of leads to be employed would be six, namely, leads 1 to 3, V1, V4, and V6.

Answer.—It would be a good thing if every person had an electrocardiogram taken in young adult life before any heart trouble develops, particularly for future use to compare with records taken later when heart trouble may be suspected, or if taking of electrocardiograms was repeated routinely. Occasionally, such a routine electrocardiogram made during the early twenties may reveal some abnormality that had not been discovered before. Because of the current custom and because of their value, the 12 leads that are now routinely used should be obtained, that is, the three bipolar limb leads, the three unipolar limb leads, and the six unipolar chest V leads.

Answer.—Routine electrocardiograms for screening purposes may be applied to the greatest advantage in patients over age 40. Even if normal, these records will frequently be of great value as baseline studies against which subsequent changes can be evaluated. As a screening tool in mass surveys, lead 1 is highly effective in dividing a population into "normal" and "abnormal" groups. Abnormal curves are most likely to be found in leads 1 and V4 or V6. The most information can be obtained with a minimum of repetition by taking either the unipolar or bipolar limb leads together with leads V1, V3 (or V4), and V6.

STELLATE BLOCK AND CEREBRAL THROMBOSIS

TO THE EDITOR:—*What is the consensus on the value of stellate block in treatment of cerebral thrombosis or embolism? Is its use recommended in cerebral hemorrhage?*

M.D., California.

ANSWER.—The value of stellate block in cerebral thrombosis and embolism has not been demonstrated. There are instances in which it undoubtedly has a definite temporary effect, but whether there is a worthwhile prolonged effect has yet to be shown. No one would advocate its use in the presence of cerebral hemorrhage.

ABDOMINAL PAIN AFTER APPENDECTOMY

TO THE EDITOR:—*In* THE JOURNAL, *Jan. 3, 1953, page 88, Dr. Frederick Serbin comments on the remarks made by Dr. Leon J. Taubenhaus in* THE JOURNAL, *Sept. 6, 1952, page 66, on abdominal pain after appendectomy. We would like to comment on Dr. Serbin's remarks.*

We are in accord with the description of patients who have persistent pain in the lower abdominal quadrants following surgical intervention and with the opinion that such pain is often due to a segmental neuralgia. These observations were first made by John Carnett in 1926 and later by Dr. Carnett and one of us (W. B.). These facts were reviewed in "Pain Syndromes" by us. Our book includes the details of an attempt to repeat the work of Kellgren and Lewis in England, involving injection of 6% sodium chloride solution at various paravertebral levels, such as D-12 and L-1. Kellgren and Lewis make the following comment: "It will be clear from these examples that by injecting in the appropriate place such somatic structures as the interspinous ligaments with a little hypertonic saline, it is possible to reproduce pain having the segmental distribution characteristic of visceral disease, simultaneously with the superficial and deep tenderness, and the muscular rigidity, which frequently accompanies such pain (the viscero-sensory and viscero-motor reflexes of Mackenzie)."

Contrary to the observations of Kellgren and Lewis, it has been our experience that pain that is projected from an irritated musculoskeletal structure is not associated with segmental tenderness unless the irritation directly involves the nerve roots or trunks. Clinically as well as experimentally this can be seen in many forms of intrasegmental radiation; for example, pain in the hip tendons will be referred to the lower leg, simulating sciatic pain; injections of liver into the buttock may cause pain in the leg, even a cramp in the calf; hip joint pain is reflexly referred by way of the obturator nerve to the knee; and pain of tendinitis of the shoulder is referred to the lower arm. With these, we have not observed any recognizable pattern of tenderness in the area of referred pain. This was true also in the exceptional cases in which we were able to produce radiating pain with the use of hypertonic sodium chloride solution.

Concerning visceral pain, appendicitis in the early stages is not evidenced by any form of tenderness. Later, when the parietal peritoneum becomes irritated, the skin overlying the irritated parietal peritoneum develops an irregular pattern of tenderness. This irregular area of tenderness will shift according to the position of the appendix. If the tenderness were caused by an intrasegmental reflex, the areas of tenderness would be constant in location according to the anatomic distribution of the nerve and would not shift with the position of the appendix.

As a general rule, our experience with radiating pain has been as follows: When tenderness is found that has a segmental pattern it is due to nerve root irritation. When pattern tenderness is absent the pain usually has a visceral origin, or it may be reflexly referred from an irritated somatic structure. It is difficult at times to differentiate these two types of pain.

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INGROWN HAIR IN BEARD

TO THE EDITOR:—*In regard to the query on "Ingrown Hair in Beard" in the Dec. 27, 1952, issue of* THE JOURNAL, *page 1736, it may be of interest to elaborate on the answer given. About 12 years ago, there was an article in a dermatology journal explaining the cause of "ingrown hairs" and the small nodular scars in the neck region of Negroes. Men with straight hair who stretch the skin when they shave closely push the hair above the normal skin line, and, when the hair is cut and allowed to retract to its normal position, it is found to have been cut below the hair follicle opening. These hairs, when growing out again, do not always follow the hair follicle lining and grow into the side, thus setting up an ingrowing hair with localized inflammatory reaction. The prevention is in not shaving closely by stretching the skin. Men with curly hair, Negroes especially, have hair that grows out and, because of the curl, points back to the skin; if allowed to grow, the hair penetrates a nearby follicle. Then on shaving the hair is cut at the skin margin, leaving the tip of the hair in the skin. This sets up a typical inflammatory reaction. The prevention is in shaving every day and in brushing the hairs, especially those on the neck, prior to shaving.*

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POLIOMYELITIS AND CEREBRAL PALSY

TO THE EDITOR:—*I noted with some concern the Query and Minor Note regarding poliomyelitis and cerebral palsy, in* THE JOURNAL, *Nov. 29, 1952, page 1362. It was stated that no incidence of poliomyelitis with the presence of cerebral palsy has been reported and that the combination would be rare. I wonder if undue emphasis might be placed on these statements so that, in many cases, the possibility of development of poliomyelitis in children with cerebral palsy would be given less attention than it deserves. I have at least 12 patients in my own practice, which is limited entirely to cerebral palsy, in whom both conditions are present. In addition to these patients, in whom first one or the other of the conditions was present and the second one was superimposed at a later date as a result of a completely different episode, I have a larger number of patients under treatment in whom polioencephalitis has been the causative factor. In such cases in which sufficiently severe involvement is present, there will be distinct symptoms of both poliomyelitis and cerebral palsy, each requiring the specific methods of management necessary for optimum improvement.*

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TOURNIQUET FOR SNAKE BITE

TO THE EDITOR:—*In a letter in* THE JOURNAL *Nov. 22, 1952, Dr. A. H. Raynolds referred to my experiments on cold in the treatment of snake bite* (South. M. J. **31**:*1248, 1938;* Am. J. Trop. Med. **19**:*393, 1939;* Am. J. Surg. **68**:*170, 1945*). *Several other correspondents have taken no notice of this method. The local refrigeration need not prevent use of other measures, such as incision-suction and the venous tourniquet; but if these customary methods were compared with refrigeration for delay of absorption of standard substances, such as mustard gas (Yudin, S. S.:* Am. Rev. Soviet Med. **2**:*4, 1944*) *or penicillin (Trumper, M., and Hutter, A. M.:* Science **100**:*432, 1944*), *it is likely that refrigeration would prove more effective. Also, ice probably minimizes tissue damage and is certainly the best local analgesic. The method seems rational not only for black widow spider bites but also for the irritations of bee and wasp stings and mosquito bites, especially in cases of sensitivity.*

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